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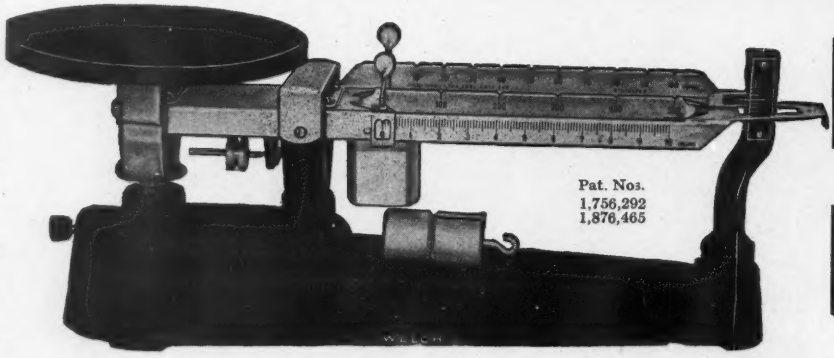

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Editor's Outlook

READIN', 'ritin', and 'rithmetic. It is a long time since our curricula were based upon these, but still the three R's are the basis of much of our education. They are means as well as ends. Certainly they have a close bearing upon the education of chemists, as of others.

If we may expand arithmetic to include all of mathematics, it has a good claim on first importance. Most of us who have anything to do with student counseling always advise the aspiring chemist to take all the mathematics he can absorb. He should not stop short of his limit, for mathematics is a language, a tool, and a discipline in which the chemist of the future must be fluent, skillful, and adept.

Reading is something which every educated person not only should be *able* to do but should do. The chemist is not to be excused from this; it should be a professional responsibility, as well as a pleasure. Much more is of course implied than the casual reading which we all do, for pleasure or necessity. Too often, students in the sciences are not expected or encouraged to read anything but their text books. The habit of wider, elective reading should be begun early. Somehow, we must provide opportunity and encouragement for this in our already otherwise busy courses.

Writing has been the ugly duckling of the family. Not mere penmanship, of course, which has long ceased to claim much attention, what with the competition of the typewriter, which may indeed some day entirely displace the laborious pen. Rather, what used to go by the unsavory name of rhetoric. And here we are missing a bet.

In the intellectual professions (and dare we include chemistry here?) most of our creations must be put into words for transmission to other minds. Strange that we should concentrate our attention upon the steps leading up to a final result and then fail to provide for the step which makes the creation really live.

Greater attention should be paid to this in the training period. Whether it concerns a laboratory exercise, a library assignment, or a piece of thesis research, we should stop speaking of the "writing up" as though it were something plastered on top of the real job. It is as much a part of the whole proceeding as the final galvanometer reading or the analysis of the product.

Students should be taught to take as much pride in the written expression of ideas as they do in the attainment of the understanding which they reveal. To be sure, writing is often hard work; it requires the real expenditure of "mental energy." But if one can get real pleasure out of mastering a difficult mathematical theorem or an intricate relationship in thermodynamics (and many do), it is not too much to hope that pleasure may be derived from the correlation of ideas and setting them out in clear words.

To say that chemists are an illiterate lot would be going too far, but there certainly seem to be few of them who have (or at least *show*) much facility in written expression. Of course, this is not a malady to which chemists alone are susceptible.

Perhaps we are too busy to do much more than *think* our thoughts. But you might be surprised how the clarity of your thinking is increased by the task of committing it to comprehensible words. Thoughts merely buzzing around won't do; they must *settle*—and *stick*. Everyone whose job is partially, if not entirely, intellectual should assign himself the regular task of some creative writing every so often.

Editors may be induced to read—perhaps even publish—what you write. However, in the name of all of them, I entreat: apply some self-censoring before expecting this.

There is no good thing which can't be done to excess; too much writing can no doubt be bad. Good examples of this could be cited from any editor's files or experience. But so can too much nutrition be bad, too much sunshine, too much going to church. So the prescription is still a good one.

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COBALT RETURNS

Increased demand for new metals and improved processes for recovering them from previous wastes brings to life a dead mining "boom-town."

COBALT, Ontario, pointed out to tourists as a ghost town for almost a quarter century, has aroused from its lethargy and now lives, thrives, and throbs again as it did in the early part of the century when it was the silver mecca of the world.

New life was breathed into the little community last fall when the United States Government increased the price of foreign silver to 71 cents an ounce, and Cobalt's pulse beat even faster when the price was again increased to 90 cents.

In 1903, workmen laying railroad track through the wilderness 300 miles north of Toronto were plagued by a lunch-stealing fox. Fred La Rose, one of the workers, threw his hammer at the fox, missed, chipped a piece of rock from the railroad siding that was almost solid silver, and started one of the greatest mining booms in history.

The Cobalt bonanza was front page news throughout the world. Fortunes were made overnight. By 1906, 44 mines were in operation. By 1916, they had produced over 300,000,000 ounces of silver, worth $150,000,000, and had paid their stockholders more than $90,000,000 in dividends. Townsite Mine, so named because its labyrinth of tunnels ran under the streets of Cobalt, was capitalized at $44,000 and made the fabulous record of paying its stockholders $1,300,000 in dividends—160 per cent per year for 16 years.

Then the price of silver dropped. At the end of World War I it had slumped to 25 cents an ounce—too low to mine, mill, and refine profitably. One by one the mines closed down until Cobalt all but died. Only a few of the former residents remained.

Now workers are moving back with their families. Twelve mines are being dewatered after being submerged for over 20 years. As water recedes from the 60 miles of tunnels under Cobalt and the countryside, geologists find that rich deposits of silver and cobalt lie untouched, ready for mining.

Two of the mines, Temiskaming and Aguanico, are already in production. Ore is being sent daily to the 100-ton mill for processing into concentrate. Thousands of tons have been bagged waiting for treatment as the giant new 10-ton smelter nears completion. Cobalt never had a smelter and shipped its ore or concentrates for recovery of the metals.

Before mining operations could begin, a vast reclamation program had to be tackled. Careless and unscientific mining methods used during bonanza days resulted in great waste and flooding of many of the mines. Early miners took out only high-grade silver ore and left behind a great wealth of ore that is considered exceptionally high grade now. Modern methods of diamond drilling and a better knowledge of geology and geophysics are uncovering additional rich ore that early operators did not discover. Engineers launched a program of dewatering the flooded tunnels.

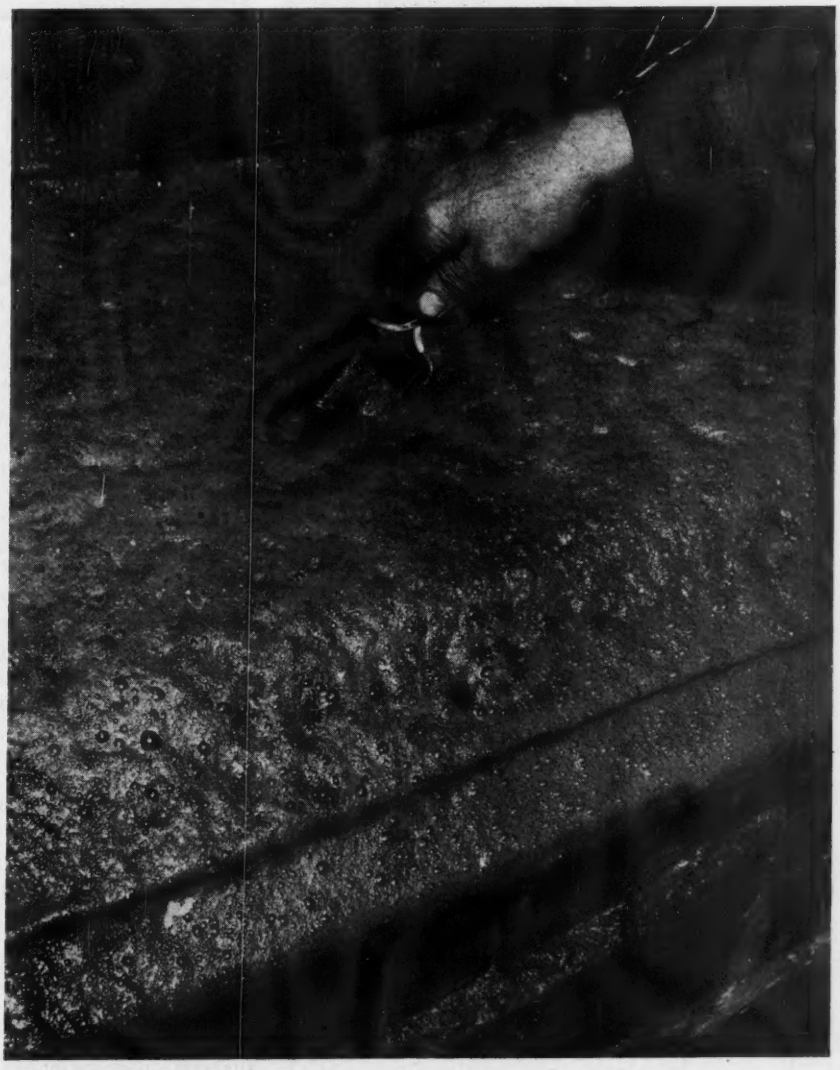
Cobalt, now a valuable metal, used in more than 300 basic industrial applications, was considered a nuisance by the early miners—something they had to remove to get at the silver. Hundreds of tons of rich cobalt ore are in refuse heaps that dot the hillsides of Cobalt and need only to be milled and refined.

Tons of ore are hoisted daily from Temiskaming and Aguanico Mines to the 100-ton mill for grinding and processing into ore concentrates. Arriving at the mill in big chunks, the ore is crushed to the consistency of talcum powder in giant, revolving drums filled with steel balls. The powdered ore is then suspended in water and run over a revolving table where the light rock powder flows off, leaving the heavier metals at the bottom. The next process, flotation, lifts the valuable metals from the pulp in the form of bubbles which flow off. Screened and dehydrated, the concentrate is ready for bagging. Thousands of tons of concentrates wait to be treated in the new smelter and refinery.

The new plant will be the largest of its kind in North America. With the facilities for smelting and refining 10 tons of silver and cobalt concentrates a day "on location," mining costs will be decreased considerably.

Efficient milling of cobalt ore, which contains up to 100 pounds of metallic cobalt per ton of mine-run ore, means recovery of from 80 to 90 per cent. The market value of mill concentrates containing 10 per cent or more of metal varies from $1.10 to $1.80 a pound.

The demand for cobalt far exceeds the supply. Besides its traditional use as a pigment for dyes, it is used as a steel hardening alloy, in electrical appliances, and in making permanent magnets. Because of its heat-resisting qualities, cobalt is used in internal combustion motors and in jet propulsion engines.



FLOTATION SEPARATOR IN WHICH METAL GOING THROUGH AN ACID BATH COMES TO SURFACE AND FLOATS OFF IN HEAVY BUBBLES. BUBBLES ARE ALMOST PURE SILVER AND COBALT.

ORE IS AGAIN MOVING THROUGH 60 MILES OF TUNNELS UNDER COBALT THAT HAVE BEEN SILENT FOR 20 YEARS.

Courtesy of Silanco Mining and Refining Company

DRILLS CHATTER AGAIN IN THE LONG SILENT COBALT MINES

Until World War II, imports of cobalt to the United States had been chiefly from the Belgian Congo and Northern Rhodesia. When the metal became critical during the war, interest turned to Canada. In the near future, Cobalt, Ontario, will be the chief source of supply of this highly valued metal for U. S. industry.

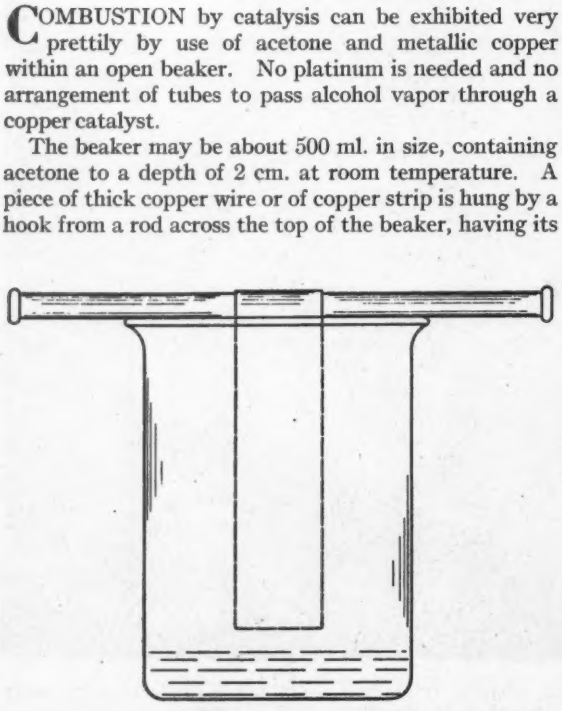
Demonstration of Combustion by Catalysis

LEON McCULLOCH

Westinghouse Research Laboratories, East Pittsburgh, Pennsylvania

COMBUSTION by catalysis can be exhibited very prettily by use of acetone and metallic copper within an open beaker. No platinum is needed and no arrangement of tubes to pass alcohol vapor through a copper catalyst.

The beaker may be about 500 ml. in size, containing acetone to a depth of 2 cm. at room temperature. A piece of thick copper wire or of copper strip is hung by a hook from a rod across the top of the beaker, having its lower end just above the surface of the acetone as shown.



To start the combustion, the copper is lifted from the beaker and is preheated to redness by holding it in the flame of a nearby Bunsen burner.

While still red-hot, the copper is suddenly placed in position above the acetone. At contact with the vapor, the oxidized surface of the copper is reduced, and catalytic combustion commences. The copper remains at red heat and brightly metallic, except for the transient flow of oxide films across its surface as the result of convection currents. The movement of these oxide films resembles that of a flickering flame. To cut down the draft of heated air, the top of the beaker can be partly covered by strips of cardboard or glass. The color effects are more striking when viewed in the dark. The combustion may continue until the acetone is all used up.

Among the products of the combustion are aldehydes, as is strongly evidenced by their odor. A test with litmus shows acid also to be present. On account of the irritating nature of the vapors, the experiment should preferably be made with good ventilation.

It seems remarkable that the acetone does not enflame or "catch fire." This is perhaps because of the unusually high ignition temperature of acetone. The experiment seems quite safe with reasonable precautions against accidents.

Atomic Size and the Periodic Table[1]

J. A. CAMPBELL
Oberlin College, Oberlin, Ohio

THE development of the techniques of X-ray and electron diffraction has made it possible in the last 30 years or so to determine the internuclear distances in many substances. As tables of internuclear distances increased in scope, Bragg, Landé, Wasastjerna, Goldschmidt, Pauling, and Huggins showed that it was possible to assign to atoms radii which might be added to give the experimentally determined internuclear distances in a wide variety of substances. These radii were subject to variation as the bonding situation varied. It is now fairly well agreed that atomic radii in compounds depend mainly on: (1) the multiplicity of the bond, *i. e.*, single, double, or triple, (2) the oxidation number of the atoms, (3) the relative preponderance of ionic or covalent bonding, (4) the coordination numbers of the atoms, and (5) the repulsion of atoms not directly bonded. It should not be thought that these criteria are completely separable, as all may apply to a given case. Thus, the first four all depend on the number of electrons and kind of orbitals available for bonding.

With at least five variables it is not surprising that the atomic radius of a given atom may change somewhat from substance to substance. Fortunately these variations are often relatively small except as affected by multiplicity and oxidation number, so that these two criteria alone may be applied in many problems of structural chemistry and the atomic radii tabulated with only these as variables.

The assignment of the radius of a neutral atom might appear in the light of the above to be a simple matter since bond multiplicity would not be serious in most cases, the oxidation number should be zero, bonds between identical atoms should be essentially covalent, and coordination numbers and atomic repulsions ought not to vary. This theoretical ease of assignment is not borne out by experiment. It is necessary to pick and choose if a "consistent" set of radii is to be obtained.

But what does one mean by "consistent?" If atomic radii were useful only in predicting crystal parameters, interest in the problem would be restricted indeed, but if it proved possible to correlate a great deal of information in terms of these values and even to predict chemical behavior from them, their value is greatly enhanced. By a "consistent" set of radii we mean, therefore, a set which not only follows X-ray and electron diffraction data but also incorporates chemical knowledge.

In assigning radii to neutral atoms, hydrogen for instance, the structural data give two values of closest internuclear distances, H—H intramolecular (covalent) and H—H intermolecular (van der Waals), which differ greatly as shown in Figure 1. Which is to be the radius consistent with those of the other atoms, such as sodium, where molecule formation does not occur? For the purpose of correlating chemical behavior of elementary substances it soon becomes obvious that the covalent distances are the desired ones, although there is insufficient space here to prove that point. In Figure 2 are shown the models of the relative sizes of the atoms and ions. The labeled spheres indicate the relative size of the neutral atoms when the single covalent or the metallic bond is used as the comparison unit. The unlabeled spheres show the size of the positive ions of the elements above and to the left as do also the spheres which are marked as representing negative ions. Metallic elements and ions are indicated by the white spheres, nonmetallic ones by the black spheres, and amphoterics by the gray spheres.

The regularities which have been pointed out by previous investigators are apparent. (1) There is a tendency for the elements in any one family (column) to increase in size as the atomic number (number of electrons) increases. (2) This family increase in size is slower as the atomic number becomes larger. (3) There is a general decrease in size along each row from left to right as the atomic number increases. (4) This decrease in size along the rows is less marked as the atomic number increases. (5) Atoms which have an upper left to lower right diagonal relationship to one another tend to have similar sizes, particularly on the left side of the table.

In addition, certain apparent discontinuities in these trends appear. (1) The inert gases show a sudden increase in radius over the halogens, and the alkali metals a further increase over the inert gases. (2) In the long

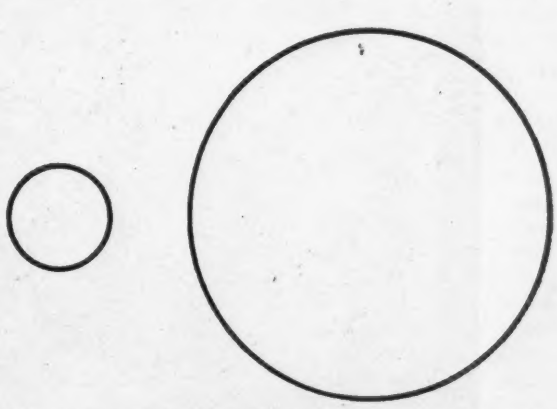
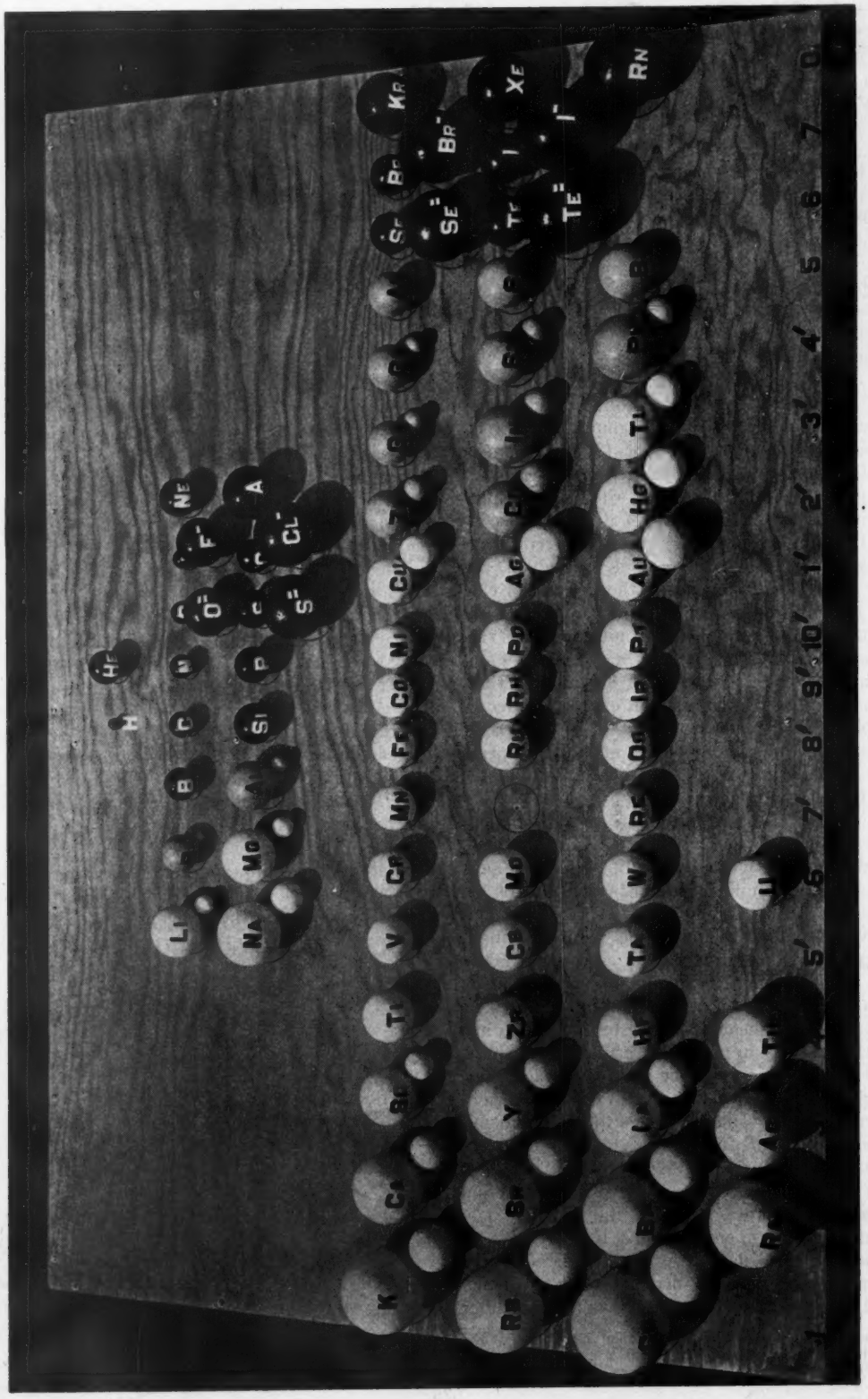


FIGURE 1.—RELATIVE SIZE OF THE COVALENT RADIUS OF HYDROGEN (AT LEFT) AND VAN DER WAALS' RADIUS OF HYDROGEN (AT RIGHT)

[1] Presented before the Division of Chemical Education at the 110th meeting of the American Chemical Society in Chicago, September 9–13, 1946.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Xe
Rn
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4
5
6
7
0

FIGURE 2

rows the gradual decrease in size exhibited by the first ten elements reverses itself and an increase occurs, followed by another decrease in radius. (3) In Columns 1, 2, and 3 there is a regular increase in size with increasing atomic number, but in Columns 4, 5′, and 6′ there is practically no change in size of the atoms between the second and third long row (*i. e.*, Zr-Hf, Cb-Ta, and Mo-W) although the differences between the first and second and between the third and fourth long rows are normal. The interpretation of the regularities and of these seeming anomalies is easy in terms of bond orbitals, but space prevents an elaboration here.

With these regularities and irregularities in mind let us apply the model to the correlation of chemical data.

METALS AND NONMETALS

Metals and nonmetals are differentiated in many ways but perhaps the most general definition is: An element is a metal if it has relatively loosely held electrons, a nonmetal if the electrons are relatively tightly held. Thus, metals act as reducing agents and form simple positive ions, reflect light, conduct electricity and heat well, have low ionization potentials, are ductile and malleable, and form basic hydroxides because of their relatively small attraction for electrons. Nonmetals owe their properties to their relative tendency to acquire electrons.

We then arrive at two familiar rules of chemical behavior in terms of size (*i. e.*, covalent radius) alone. (1) The bigger an atom, the farther from the nucleus are the valence electrons and hence the more metallic the atom. (2) If two atoms have the same size, the one with the larger atomic number (nuclear charge) is less metallic. Nonmetallic elements are those with small atoms and high nuclear charge.

As the atomic number increases in any row, the electrons are attracted more strongly to the nucleus, the size in general decreases, and the atom becomes less and less metallic. As the atomic number increases in the alkali metal family, the size also increases, and the two effects counter one another with the size effect predominant so that cesium has the lowest ionization potential, *i. e.*, is most metallic. However, in all the columns from Ti-Hf to Ga-Tl the increase in size is not sufficient to offset the increase in nuclear charge and in all these columns the most metallic element is at the top. In the last five columns (4′, 5, 6, 7, and 0) the increase in radius again more than offsets the larger nuclear charge, and the most metallic element is that of highest atomic number in each column. In the Ge, Sn, and Pb family the two effects almost balance, and these three elements have similar metallic and nonmetallic properties.

ACIDIC OR BASIC NATURE OF THE ELEMENTS IN COMPOUNDS

A practical example of this correlation may be found in the analytical separation of copper, cadmium, bismuth, arsenic, mercury, tin, and antimony from a mixture of their sulfides. Treatment of the mixture with sodium sulfide solution will dissolve out the most acidic sulfides (the sulfides of the smallest atoms with relatively high nuclear charges, *i. e.*, the nonmetals). As_4S_6 and Sb_4S_6 dissolve in this reagent. Examination of the periodic table shows these the most acidic by reason of their small size. If the solution is made more basic, the HgS dissolves whereas one would predict on position in the periodic table alone that SnS should dissolve next; however, the higher nuclear charge of the mercury makes the HgS more acidic than SnS. If the SnS is now oxidized to the plus four state, SnS_2, it will dissolve since the higher oxidation state makes the tin more acidic (holds electrons more tightly). This is a standard method used in dissolving the arsenic, antimony, mercury, and tin sulfides, leaving copper, cadmium, and bismuth in the solid sulfide state. It might be noted that any arsenic and antimony present as plus five or mixed sulfides would dissolve most readily because of their higher oxidation states.

It should be pointed out here that size and nuclear charge are not sufficient criteria to correlate all cases of variation in metallic nature since electronic structure is even more fundamental. It is electronic structure which accounts for the anomalous behavior of copper compared to nickel and zinc. Fortunately size is a rather sensitive function of electronic structure so that much correlating is possible in terms of size alone.

The effect of change in oxidation number on acid-base reactions may be illustrated by the separation of chromium, manganese, iron, cobalt, and nickel. Treatment of a solution containing Cr^{+++}, Mn^{+++}, Fe^{+++}, Co^{++}, and Ni^{++} with a solution of ammonia precipitates the Cr^{+++}, Mn^{+++}, and Fe^{+++} but not the Co^{++} or the Ni^{++} since the ions of the higher oxidation state are both smaller and more highly charged and, therefore, more acidic. If the Mn^{+++} is reduced to Mn^{++}, it then no longer precipitates but remains in solution with the Co^{++} and Ni^{++}, for the lower oxidation state is not sufficiently acidic to react with the weak base.

RELATIVE STABILITY OF OXIDATION STATES

The electronic structure determines primarily what oxidation states a given element will exhibit, but the relative stability of these states is often best correlated with the nuclear charge and size of the element. In the nitrogen, phosphorus, arsenic, antimony, bismuth group, for instance, the most stable oxidation states are -3, $+3$, and $+5$. The stability of the -3 state decreases with increasing atomic number, the stability of the $+3$ state increases with increasing atomic number, and the stability of the $+5$ state is a maximum with phosphorus. On the basis of electronic structure and bond orbitals alone these facts are inexplicable, but a brief examination of the nuclear charge-size relationships allow a good correlation to be made. The atomic radii in this group increase in a regular fashion as the atomic number increases, with the rate of size increase great enough to overcome the increasing nuclear charge, and the elements become more and more metallic from

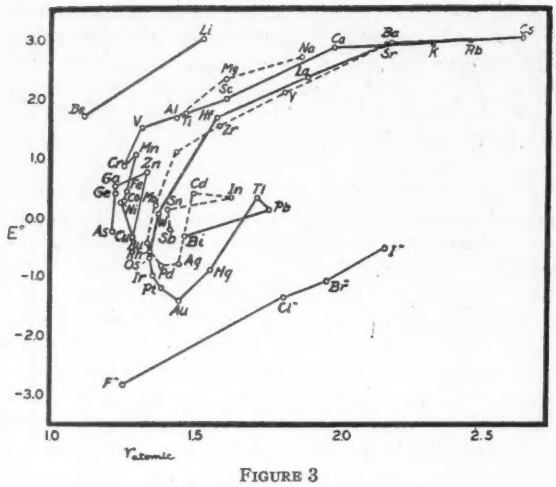

FIGURE 3

nitrogen to bismuth. Thus nitrogen is most nonmetallic and bismuth most metallic. Nitrogen, therefore, is able to acquire electrons (by sharing) relatively more readily than bismuth, while bismuth is relatively more willing to form a simple positive ion by losing electrons. Since the -3 and $+5$ oxidation states are attained only by sharing electrons in covalent bonds, the more nonmetallic elements of lower atomic number favor these states. The $+3$ state on the other hand may be strongly ionic so that bismuth is most stable in this state while the lower atomic numbers are relatively less so. (The reason the $+5$ phosphorus is more stable than $+5$ nitrogen involves the greater number of bonding orbitals available in the phosphorus with the resultant formation of stronger bonds here than in nitric acid).

Similar correlations may be applied to the other families as well as to the row relationships in the periodic table.

OXIDATION-REDUCTION POTENTIALS

The standard electromotive series of the elements offers further evidence for the effect of size and nuclear charge on chemical properties. The reducing power of a substance in aqueous solution depends on many properties, but each of these properties is in turn a function of radius and nuclear charge, so that a plot of E^0 against r_{atomic} shows a good correlation. In Figure 3 an E^0 against r_{atomic} plot shows the effect for each row of the periodic table. Lithium and beryllium are much better reducing agents than would be predicted from the size of the neutral atom because of the very high hydration energy of the small ions formed. This hydration effect stabilizes the ions and increases the reducing power of the metal. As the nuclear charge increases, the elements tend to become poorer reducing agents unless the smaller size and higher nuclear charge in the ion provide a counterbalancing hydration energy. The large decrease in reducing potential as the atomic number increases in Groups 1′ and 2′ should be particularly noticed, together with the fact that while Zn and Cd are the best reducing agents in their rows in this region of the periodic table, Tl is the best in its row for the same region. This follows from the shift in maximum radius from Group 2′ to Group 4′ as the atomic number increases.

It should also be noted that there are few exceptions within the columnar families to the rules previously stated concerning metallic nature—and therefore reducing power. Lithium is the only notable exception, and owes this to its high hydration energy compared to the other alkali metals.

The halide ions as reducing agents also fit into this system. An E^0 versus r_{ion} plot gives an almost straight line. That this line does not coincide with that of the metals is not surprising in view of the different nature of the electrode processes.

SOLUBILITY OF SALTS

The extent of the solubility of an electrolyte in water involves many variables also, but here again most of these variables are functions of the sizes of the ions and the nuclear charges so that a good correlation may again be obtained if the solubility is studied as a function of ionic size alone. In this case, since both positive and negative ions are present, two sizes must be considered. In the case of a one-to-one electrolyte (alkali metal halides and hydroxides, alkaline earth sulfates, etc.) the correlations are simple. If there is a great disparity in the size of the ions, the stability of the crystal decreases because the small ions are not big enough to keep the large ions separated. As the large ions approach one another more and more closely, mutual repulsions increase and the crystal becomes more soluble. The solubility of cesium fluoride is 1000 times that of lithium fluoride, due mainly to the increasing repulsion of the positive ions as their size increases while that of the negative ion remains constant. The alkali metal hydroxides likewise increase in solubility from lithium to cesium. In the alkali metal iodides, saturated lithium iodide is seven times as concentrated as saturated cesium iodide, due to the decreasing negative-ion repulsion as the positive ions become bigger. Further, there is a regular decrease in solubility in the alkaline earth sulfates from beryllium to radium for the same reason. Maximum stability of the crystal, and hence minimum solubility, does not occur when the ions are the same size, but rather when the negative ion is from one and one-third to twice as large as the positive ion. This results to a large extent from the polarization of the negative ion by the positive ion, which increases crystal stability. The smaller the positive ion, the greater this stabilizing influence. With one to two electrolytes (alkali metal sulfates and alkaline earth halides and hydroxides) it is necessary to consider the double effect of one of the ions, but the general principle holds. Thus, the solubilities of the alkali metal sulfates show a minimum for potassium, increasing both as atomic number increases and decreases, while the alkaline earth hydroxides increase in solu-

bility with increasing atomic number in a regular manner.

CONCLUSION

These few examples illustrate only a small portion of the data which may be correlated in terms of this atomic size model of the periodic table. If electronic structures are considered at the same time, it is possible to correlate and predict the properties of weak electrolytes, complex ions, melting points, boiling points, densities, ionization potentials, hardness, color, etc. Exceptions are plentiful, but the immense amount of data which may be correlated far overcomes this ever-present drawback.

The correlation of size and chemical properties is particularly valuable in the teaching of elementary chemistry, for the beginning student may now see some simple physical interpretations for variance in chemical behavior. In advanced courses the more fundamental concepts of electronic orbitals amplify this simpler correlative approach and, in fact, allow a rather complete interpretation of the factors determining the size of a particle. Size is not the last word in the interpretative approach to chemistry, but it serves as a convenient further step in removing chemistry from the encyclopedic pedantry of the alchemist.

Thanks to the workers in X-ray and electron diffraction, chemistry is much closer to being an exact science than most of today's textbooks indicate.

Industrial Uses Of Phosphates

PAUL LOGUE

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THE active participation of phosphorus in World War II has done more than a whole library of books to create in the common man an awareness of this element. Although it has always been a part of his body and is essential to his nourishment and well being, he has never before become so conscious of its potentialities for good or evil.

Phosphorus, bearer of light, was reputedly discovered accidentally in 1669 by Hennig Brand, an impoverished German merchant, who sought to restore his wealth by converting base metals into gold. Could he have visualized the tremendous significance of his discovery, he would hardly have been willing to dispose of it as he did for 200 thalers, for its tremendous utility is modern life makes it one of the most valued elements in our chemical storehouse.

Fertilizers are the oldest application of phosphorus and continue to represent the largest tonnage, but in the so-called refined phosphorus salts, virtually a new chemical industry has been brought into being.

Phosphorus produced in its elemental form from phosphate-bearing ore is the mother element of this new industry and growing family of phosphates. Today most of the food-grade phosphoric acids and phosphates, other than those used for fertilizers, are produced by processors of elemental phosphorus from electric furnace operations. Huge electric furnaces feed power through carbon electrodes, tearing phosphorus free from the molecules in which it is held and extracting it in substantially pure form. From phosphorus burned in air comes phosphoric acid, and from this versatile compound are derived the modern phosphates which reach into almost every basic industry.

Widely varied are the uses of phosphates in food manufacture and in the preparation of foodstuffs. In sugar refining, for instance, phosphoric acid is employed in conjunction with lime as a clarifying agent of raw sugar syrup, which contains albuminous and other protein matter. When lime and phosphoric acid are added, they react to form calcium phosphate which precipitates out, carrying with it the protein impurities.

In gelatin, phosphoric acid is added as a refining agent, and in jellies it functions in controlling the jelling action through maintenance of the pH at the required level. In jellies, as well as in soft drinks, phosphoric acid is an acidulant to replace fruit acids, such as citric or tartaric.

Of daily increasing significance in the foodstuffs preparation are mono-calcium phosphate and sodium acid pyrophosphate, acting as acid leavening agents in the leavening of self-rising flour, cakes, biscuits, and bakery sweet goods. Both chemicals release carbon dioxide from baking soda. The residual salts left after the leavening function is complete, in turn, serve as nutrient elements in body nourishment. As each adult contains in his system approximately 1.4 pounds of phosphorus, he requires a continual replenishing supply.

Both tetra-sodium pyrophosphate and di-sodium phosphate are used as small additions in dairy products and have done much to make possible the fast growing packaged cheese industry. Packaged cheese must be made from natural cheeses whose characteristics vary widely. Such cheeses sometimes tend to give off their fat, and, as a result, globules of oil form on their surfaces. Emulsifying agents such as tetra-sodium pyrophosphate and di-sodium phosphate are used to prevent this so-called "oiling off."

Di-sodium phosphate is also used in the adjustment of calcium phosphorus ratios in prepared milk and ice cream. Its action is as an emulsifier, tending to prevent agglomeration of solids, and insures a smooth, creamy consistency.

To fortify foodstuffs, such as flour, ferric phosphate provides a rich source of iron. This compound is stable, offering no deleterious effect on the product with which it is associated. Tri-calcium phosphate has long been used as an anti-caking agent in salt, sugar, and other granular products.

Indirectly, phosphoric acid makes a contradiction to nature in its use as an ensiling agent to keep green fodder crops green. Through its use, it is possible to preserve green crops in silos with a minimum loss in nutritional value, thus affording a palatable midwinter salad for the bovine milk producer.

Related to the uses of phosphates as diet supplements are the time-honored uses of phosphates in medicinals and pharmaceuticals. The first commercially manufactured phosphate salt was di-sodium phosphate. The same compound is used today as an ingredient of saline laxatives offered under various trade names. Because of its value in dentifrices as a polishing agent, di-calcium phosphate is of special interest. Tri-calcium phosphate and insoluble sodium *meta*-phosphate are employed for similar purposes. Effective polishing agents, they do not cause wear on the tooth enamel. In addition, di-calcium phosphate serves as a source of calcium and phosphorus, correcting these deficiencies in human nutrition.—Reprinted from *Food Materials and Equipment* (April, 1946).

INFLUENZA VIRUS[1]

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ACCORDING to textbooks on medicine, the disease, influenza, has been recognized for many centuries. Medical historians refer to epidemics during the Middle Ages. The first epidemic recorded in America is said to have been in 1647. Sporadic outbreaks are fairly common, minor epidemics occur very frequently, and serious pandemics seem to occur about three or four times in a century. The disease is usually mild, but occasionally extremely severe forms of it are experienced. During the pandemic of 1918–19, it is estimated that from 6 to 15 million people died as a result of influenza. Some authorities place the death figure in the United States alone at about half a million. Even total war practiced on a global scale has difficulty competing with that record.

The cause of influenza has only recently been determined with reasonable assurance. It is generally believed that the ancients attributed the disease to the influence of the constellations. In fact, etymologists tell us that the word, "influenza," owes its origin to this belief. During the pandemic of 1892 Pfeiffer isolated a bacterium from patients suffering with the disease and regarded this organism as the causative or etiologic agent. This bacterium, whose generic name is *Hemophilus influenzae*, is familiarly known as the Pfeiffer bacillus. Even though difficulty was experienced from the first in producing experimental influenza with this organism, it was still regarded as the causative agent as late as the pandemic of 1918. At that time a great deal of experimental work was done, and it was found that the Pfeiffer bacillus could be isolated from many patients but definitely not from all. It could also be obtained occasionally from healthy individuals. Therefore, the acceptance of this organism as the prime causative factor became untenable.

A single observation was made during that pandemic which provided the clue to the solution of the cause of influenza. Dr. J. S. Koen, an inspector in the Division of Hog Cholera Control of the Bureau of Animal Industry, observed a similar disease among the swine of Iowa. Because of its resemblance to influenza, it was called "swine influenza." This marked a real step forward, for here was a disease which could be studied experimentally. In 1931 Dr. Richard E. Shope of the Rockefeller Institute showed that swine influenza could be transmitted from one hog to another by means of a bacteria-free filtrate (*1*). This observation indicated that swine influenza is caused by a filterable virus —that is, by an agent small enough to pass through a filter which will retain ordinary bacteria. However, this experimental influenza was not as severe as the natural disease. Later, Shope showed that in the natural disease a strain of the Pfeiffer bacillus, called *Hemophilus influenza suis*, plays a cooperative role. When hogs were infected with both the virus and the bacillus, typical influenza resulted. In other words swine influenza is the result of the simultaneous infection with influenza virus and influenza bacillus.

All this was known in 1931, but the cause of human influenza was still unknown. Indeed, it could only be surmised that the swine disease really was related to the human disease. However, in 1933, Smith, Andrewes, and Laidlaw in England showed that a disease could be transferred to the ferret from human patients suffering with influenza (*2*). It was next shown that this ferret disease could be transmitted from one experimental animal to another by means of a bacteria-free filtrate. Therefore, the causative agent can be presumed to be a virus. Next, it was learned that ferrets developed an immunity and that the serum from an immune ferret could neutralize the virus. Also, it was shown that the serum from man recovered from influenza would neutralize this ferret virus. Thus, the presumed relationship between the ferret virus disease and human influenza was strengthened.

It remained only to prove beyond doubt that the causative agent of this experimental disease is also the causative agent of human influenza. This was done by producing experimental human influenza with it, first in Russia by Smorodintseff and associates (*3*), later in Australia by Burnet and Foley (*4*), and finally by Henle, Henle, and Stokes of Philadelphia (*5*). It was not found necessary to introduce the Pfeiffer bacillus simultaneously in order to produce human influenza. Because of the thrice demonstrated ability to produce influenza in man by the virus perpetuated in experimental hosts, there is now no reasonable doubt that this virus is the principal etiologic agent of influenza.

Thus far, at least two distinct types of influenza, influenza A and influenza B, are generally recognized (*6*). The diseases are similar; they are both caused by viruses of similar characteristics, but they are immunologically different. Swine influenza has been shown by Andrewes, Laidlaw, and Smith, by Francis and Magill, by Shope, and by others to be related immunologically to human influenza A. This vindicates the faith of the early experimenters, who assumed that swine influenza was related to the human disease.

Progress in the study of influenza in the laboratory has been possible largely because of three important discoveries. The first of these was the transfer of the virus from the ferret to the common laboratory white mouse, first accomplished by Andrewes, Laidlaw, and Smith (*7*). Later it was transferred directly from man to the white mouse. This discovery represents a distinct advancement, for the white mouse is a cheap and convenient experimental animal.

The second important finding was that influenza virus can infect chicken embryos. This discovery has

[1] A lecture presented before the New England sections of the American Chemical Society, May 8–11, 1946.

an interesting history. In 1931 Woodruff and Goodpasture of Vanderbilt University discovered that fowl pox virus would grow on the chorio-allantoic membrane of the chicken embryo (*8*). Later they found that cow pox would also grow on this membrane. This opened an entirely new approach to the study of viruses. In 1936 Burnet of Australia found that influenza virus could be propagated on the chorio-allantoic membrane. Then in 1941 he found that the virus would be propagated if merely introduced into the extra embryonic fluids (*9*). The virus injected into these fluids finds its ways to the embryonic respiratory tract, causes a fatal disease, and in so doing multiplies and is returned to the extra-embryonic fluids. This discovery provided an extremely simple method of cultivating influenza virus in large quantities.

The third discovery was made by Hirst of the Rockefeller Foundation (*10*) and by McClelland and Hare of Toronto (*11*). They found in 1941 that influenza virus had the ability to agglutinate the red blood cells of chickens and of some other animals. This provided a simple method for the detection of influenza virus. In 1942 Hirst and Pickels contributed greatly to progress by showing that this red cell precipitation reaction could be adapted to the quantitative estimation of influenza virus concentration with an accuracy of 10 to 20 per cent (*12*).

Purified influenza virus for study in the laboratory is generally obtained by inoculating ten-day chicken embryos—or half-hatched eggs—with virus, then incubating two days. During this time the virus multiplies and finds its way back into the extra-embryonic fluids. The embryos are then chilled and opened. The fluid containing the virus is drained off.

The virus can be removed from this fluid in either of two ways: by adsorption from a cold solution with chicken red cells (*13*) or certain inorganic adsorbents, and by high-speed centrifugation (*14*). If it is precipitated by red cells, it must be recovered later by suspending the precipitated red-cell-virus complex in a salt solution at body temperature. The virus dissociates from the red cells at this temperature, and the latter are removed by low-speed centrifugation.

If the virus is precipitated from the embryonic fluid by high-speed centrifugation, it collects in a jelly-like mass at the periphery of the centrifuge. This can be suspended in a small volume of salt solution, and large particles contaminating the virus can be removed by centrifugation of the concentrate at moderate speeds.

A study with the electron microscope carried out by the writer in cooperation with Dr. Stanley (Figure 1) revealed three kinds of particles in an influenza virus preparation—very small granules, medium-sized spheres, and large clumps (*15*). The ultracentrifuge and other physical procedures yield evidence of a fourth kind of matter, a constituent normally found in the chicken embryo, composed of thread-like molecules too thin to be seen with the electron microscope. Extensive studies carried out with the ultracentrifuge and the Tiselius electrophoresis apparatus have shown that the

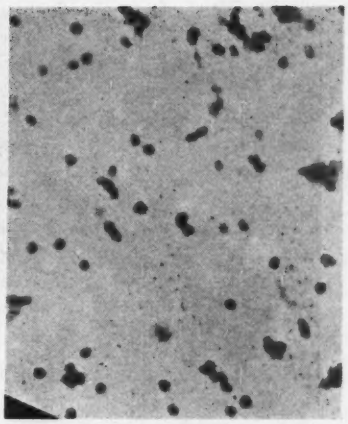

FIGURE 1.—ELECTRON MICROGRAPH OF PR 8 INFLUENZA A VIRUS MOUNTED AT A CONCENTRATION OF 10^{-4} GRAMS PER CC. IN DISTILLED WATER. × 28,200. FROM LAUFFER AND STANLEY (*15*)

ability to agglutinate red blood cells and the ability to infect mice and chicken embryos both migrate in centrifugal and electric fields at rates indistinguishable from those of the medium-sized spheres and clumps of spheres, but very different from those of the other components (*16, 17*). Fractionation experiments carried out by Stanley show that the highest specific activities always accompany those preparations with the highest relative concentration of these medium-sized spheres and their clumps (*18*). Knight isolated influenza virus from the lungs of infected mice (*19*). His preparation was found to contain similar spheres. Thus, there seems to be little room for doubt that these spheres are the actual bearers of influenza A virus activities.

From the micrograph reproduced as Figure 1 and from the magnification factor, it was possible to measure both the sizes and the distribution of sizes of the spherical particles. The mean diameter was found to be about 116 millimicrons. These particles are not all of exactly the same size. The distribution of particle sizes is shown in Figure 2. Here the number of particles at different size levels is plotted against the size. A more or less continuous distribution results. From this it is possible to calculate that the standard deviation of the distribution of particle diameters is 15 per cent of the mean diameter.

Image formation with the electron microscope depends upon the fact that matter scatters electrons. An object opaque to electrons is one which scatters them and thus prevents their transmission to the image. The electron scattering power of a material depends upon its density. Viruses have a low density, therefore a low

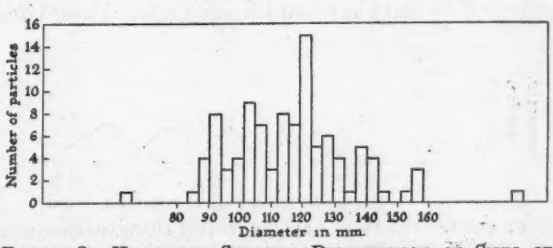

FIGURE 2.—HISTOGRAM SHOWING DISTRIBUTION OF SIZES OF PR 8 INFLUENZA A VIRUS PARTICLES

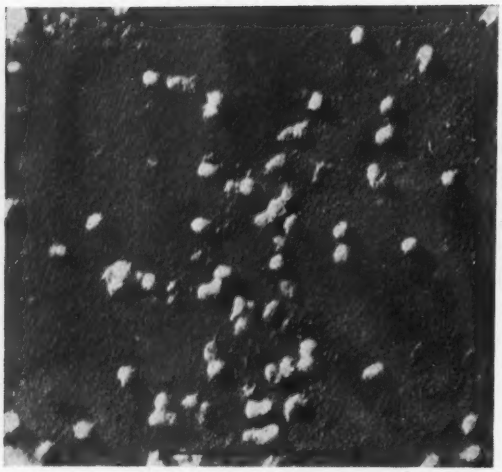

FIGURE 3.—ELECTRON MICROGRAPH OF PR 8 INFLUENZA A VIRUS SHADOWED BY THE OBLIQUE DEPOSITION OF A THIN LAYER OF CHROMIUM. FROM WILLIAMS AND WYCKOFF (*20*)

scattering power and a low opacity to electrons. This results in poor contrast between the image of a virus and the background formed by the supporting membrane. Recently a new technique has been developed wherein a very thin film of metal is evaporated on virus particles contained on the supporting membrane. The metal is evaporated at an angle to the surface. When such a metal-coated preparation is micrographed, the effect is the same as that obtained by photographing a landscape with oblique illumination. Figure 3 is a negative of some influenza virus particles plated with chromium in the manner just described and micrographed by Williams and Wyckoff (*20*). The virus particles stand out in relief, appearing as true spheres and not as circles.

With the electron microscope it was possible to learn something of the external physical nature of influenza virus particles. But little was learned about the internal structure. For this, it is necessary to turn to the ultracentrifuge. When an experiment is carried out in an ultracentrifuge, a small quantity of a solution of the material to be studied is placed in a transparent cell which fits in a hole in the rotor of the centrifuge located at some distance from the axis of rotation. The centrifuge is then spun at a high speed. If the solution under study is that of a virus, the virus particles will move through the liquid toward the periphery of the centrifuge. If the particles are all more or less alike, they will all move at about the same rate. Those virus

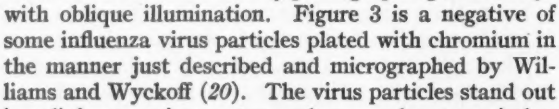

FIGURE 4.—TRACINGS OF SEDIMENTATION DIAGRAMS OBTAINED BY THE SVENSSON SCHLIEREN METHOD ON PR 8 INFLUENZA A VIRUS. FROM LAUFFER AND STANLEY (*15*)

particles originally at the top of the solution—that is, nearest the axis of rotation—will move toward the periphery at the same rate as all of the others, but there will be none to follow them. Therefore, they will constitute a boundary between the virus solution and solvent. This virus boundary moves at the same rate as each virus particle.

It is possible to take pictures of a sedimenting boundary during the course of an ultracentrifuge experiment by using one of several specialized techniques. Such a boundary between a virus solution and solvent is never infinitely sharp. If some of the virus particles move just a little faster than others in the boundary region, the boundary will become slightly foggy. There are also other causes for boundary fogging, but they do not apply in the case of influenza virus. In Figure 4 the results of an ultracentrifugation experiment on influenza virus are shown. The boundary between virus solution and solvent is represented by a peak. The center of the peak tells where the center of the boundary is at a given time, and the sharpness of the peak tells how foggy the boundary is. The successive peaks represent the boundary at five-minute intervals after the experiment was started. From the displacement of the peak centers and the speed of the centrifuge, the sedimentation constant, defined as the sedimentation rate in unit centrifugal field, can be calculated. A value of 722×10^{-13} cm. per second per unit field, or 722 Svedberg units, is obtained. From the progressively greater breadth of the curves it is possible to determine the degree of boundary fogging, and from that to get an idea of the degree of inhomogeneity of the virus.

The rate at which a spherical particle, like that of influenza virus, sediments depends upon its size and upon the difference between the density of the particle and that of the solvent. Therefore, if in addition to the sedimentation constant the density of influenza virus is known, its size can be determined. In practice one determines the reciprocal of the density—the specific volume—from measurements of the densities of the virus solution and of the pure solvent. The weighted average of six determinations of the specific volume is 0.79 cc. per gram, corresponding to a density of 1.26 grams/cc. This is the density of completely dried influenza virus. With this figure and the value of the sedimentation constant it is possible to calculate that the diameter of the influenza virus particle is 70 millimicrons. The discrepancy between this value and that obtained with the electron microscope could be attributed to either of two possible causes. First, the assumption that the particles are spheres could be wrong; however, this is extremely unlikely in view of the results obtained with the electron microscope. Second, the density of the particles in solution might not be as great as in the dry state—that is, the influenza particle in suspension might soak up a certain amount of water, thereby increasing its size and decreasing its density. This idea seems plausible, and it can be tested by using the ultracentrifuge.

The rate of sedimentation of a particle suspended in a

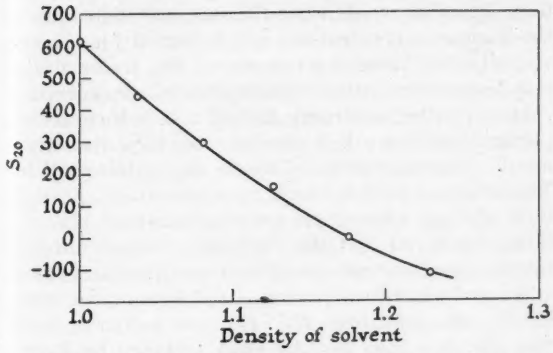

FIGURE 5.—SEDIMENTATION RATE IN SVEDBERG UNITS OF PR 8 INFLUENZA A VIRUS DISSOLVED IN SUCROSE SOLUTIONS PLOTTED AS A FUNCTION OF THE DENSITY OF THE SUSPENSION MEDIUM. FROM LAUFFER AND STANLEY (*15*)

solvent is directly proportional to the difference between the density of the particle and the density of the solvent. Thus, if influenza virus particles were suspended in a solvent with density equal to that of the virus, they would fail to sediment, no matter how fast the centrifuge was run. Also, if the particles were suspended in a medium more dense, sedimentation would take place in a reverse direction, just as in the case of cream in a separator. In fact, when the sedimentation rates of the particles measured in several solvents of different densities are plotted against the densities of the media, one should get a straight line, provided the particles have the same density in all the media. Figure 5 presents the results of an experiment in which the sedimentation rate of influenza virus dissolved in sugar solutions of various densities was studied. Here is plotted the sedimentation rate of the virus against the density of the solvent. When the density of the solvent is less than 1.18, the virus sediments toward the periphery of the centrifuge; in a solvent with a density equal to 1.18, it does not sediment at all; and in solvents more dense than 1.18, it moves in the opposite direction toward the axis. This experiment shows quite clearly that the density of a virus particle is 1.18 when it is suspended in a sugar solution with a density of 1.18. It must be remembered that in the dry state the density of the virus particles is 1.26. Therefore, in solution the virus must contain some water.

There is something peculiar about these results, however. If the density of the virus particle remains constant, one should get a straight line when sedimentation rate is plotted against solvent density; but here a curved line was obtained. This is evidence that the density of influenza virus is not a constant but changes with changes in the sugar content of the surrounding medium. This suggests that, in solvents containing very little sugar, the density of the virus is even less than 1.18. In other words in the presence of low sugar concentration, the virus contains more water than in the presence of high sugar concentrations. The density of the virus particle in a solvent free of sugar can be estimated by drawing a straight line tangent to the curve at the point representing zero sugar concentration. This line will intersect the zero level of sedimentation rate at a point corresponding to the density of the sugar solution in which the virus would float if the virus did not increase in density as the sugar concentration increases. One finds a value of about 1.1, showing that the density of the virus in a solvent free of sugar is about 1.1. A possible reason that the virus density increases as the sugar content is increased is that the sugar solution draws water out of the virus because of its high osmotic pressure. The higher the sugar content, the more water is drawn out. A more accurate way of determining the density of the virus in solution is to utilize a material for varying the density of the medium which does not affect the osmotic pressure. Sharp and other associates of Dr. Beard at Duke University (*21*) utilized a protein, serum albumin, for this purpose. Their data are shown in Figure 6. Here sedimentation rate of influenza virus is plotted against solvent density. This time the data fall on a straight line. They indicate that in a solvent of density 1.10, the virus would not sediment. Therefore the density of the virus in solution is 1.10. This result is accurate to at least one decimal place more than the one obtained from the study using sugar solutions. It clinches the argument that influenza virus contains an appreciable amount of water when it is suspended in an aqueous medium. From the sedimentation constant and the wet density of 1.10, it is possible to calculate that the diameter of the wet influenza particle is 114 μ. Also, from the wet density, the dry density, and the density of water, it is possible to calculate that the wet influenza virus particle contains 60 per cent by weight of water.

During the course of the ultracentrifugation study being described, more than a hundred analyses on many preparations of PR 8 and other strains of influenza virus were made. It was found that the values for a given strain varied widely; therefore, an attempt was made to determine some of the factors responsible for this variation. It had been known for several years that the sedimentation rate of tobacco mosaic virus depends upon the virus concentration (*22*). This led to

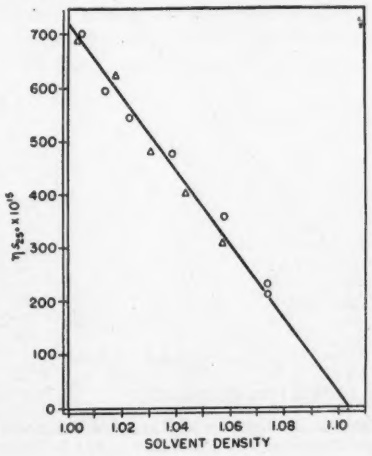

FIGURE 6.—SEDIMENTATION RATE OF PR 8 INFLUENZA A VIRUS PLOTTED AS A FUNCTION OF THE DENSITY OF THE BOVINE SERUM ALBUMIN SOLUTIONS USED AS SUSPENSION MEDIA. FROM SHARP, *et al. Science* (*21*)

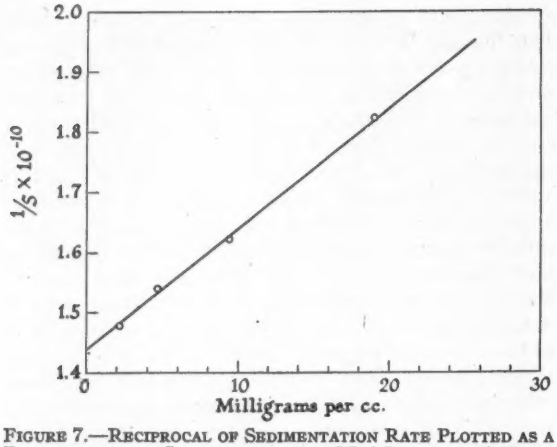

FIGURE 7.—RECIPROCAL OF SEDIMENTATION RATE PLOTTED AS A FUNCTION OF THE CONCENTRATION OF PR 8 INFLUENZA A VIRUS

an investigation of the possibility that some of the variation observed for influenza virus might also be due to concentration. In Figure 7 the reciprocal of the sedimentation rate of influenza A virus is plotted against concentration. It can be observed that the sedimentation rate is strongly dependent upon concentration. The true sedimentation constant can be obtained by extrapolating to zero concentration. In the case of tobacco mosaic virus it had been found that the dependence of sedimentation rate upon concentration could be attributed to the viscosity of the virus solution. When the sedimentation rates observed at the various concentrations were corrected for the viscosities of the solutions, the strong dependence largely vanished. This led to an investigation of the solution viscosity of influenza virus. The results are shown in Figure 8. It is evident that this material has a high viscosity. Furthermore, the viscosity is of exactly the right magnitude to account for the dependenceof sedimentation rate upon concentration. In other words when the sedimentation rates at the various concentrations are corrected for solution viscosities at those concentrations, the sedimentation rate becomes a constant independent of concentration.

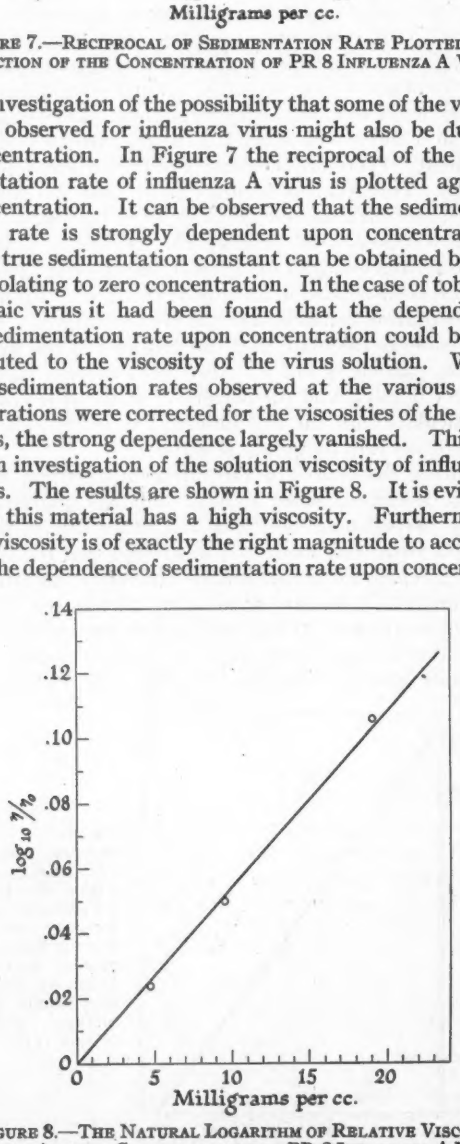

FIGURE 8.—THE NATURAL LOGARITHM OF RELATIVE VISCOSITY PLOTTED AGAINST CONCENTRATION OF PR 8 INFLUENZA A VIRUS

It was rather surprising to find that influenza virus preparations had a high viscosity, for high viscosity is usually associated with rod-like or thread-like particles. The influenza particles seem to be essentially spherical, if the electron micrographs are to be believed; however, it was observed that the PR 8 preparations obtained by the usual methods contained small amounts of an additional constituent, one that sediments more slowly in the ultracentrifuge (*15*, *17*). A similar material was obtained from healthy chick embryos by Knight (*23*). Through the courtesy of Dr. Knight, it was possible to measure the viscosity of several preparations of this normal material. It turned out to be extremely viscous. Thus it appeared probable that the high viscosity of influenza virus preparations could be due largely to the presence of a small amount of the more slowly sedimenting contaminant. This proved to be the case. A crude preparation of virus, one obtained by the usual method, was subjected to a very exacting centrifugal fractionation. Ultimately two fractions were obtained, one called the light fraction and the other the heavy fraction. The light fraction showed double boundaries in the Tiselius apparatus and in the ultracentrifuge, but the heavy fraction showed only a single boundary in each. These results are shown in Figure 9 and Figure 10.

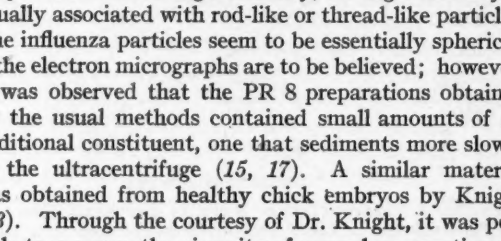

FIGURE 9.—TRACINGS OF LONGSWORTH SCANNING DIAGRAMS OF ASCENDING BOUNDARIES OF PR 8 INFLUENZA A VIRUS FRACTIONS OBTAINED IN ELECTROPHORESIS EXPERIMENTS. FROM MILLER, LAUFFER, AND STANLEY (*17*)

(*a*) Crude unfractionated virus, (*b*) heavy centrifuge fraction, (*c*) light centrifuge fraction.

It was observed, further, that the light fraction had a higher viscosity than the original and the heavy fraction had a much lower viscosity. Thus, it would seem that the contaminating material is largely responsible for the high and variable viscosity and in turn for the variable sedimentation rates. The minimum viscosity obtained for a PR 8 influenza virus preparation is still slightly higher than one might expect it to be. According to the Einstein equation, which has been well verified, the ratio of the relative viscosity increment imparted to its solution by a substance to the volume fraction of that substance should be 2.5 for spherical particles. Actually, the value obtained for the frac-

tionated virus preparation was 11.3. The simplest explanation is that the virus particles occupy a volume in solution equal to 11.3/2.5 or 4.5 times their volume in the dry state. If the virus particles in solution are made up of roughly 78 per cent water and 22 per cent solids on a weight basis, the observed viscosity would be expected. This amount of water is moderately close to that calculated from density measurements.

The isoelectric point of influenza A virus was determined by the microcataphoresis method and by the Tiselius moving boundary method (*17*). The results obtained with a very highly purified preparation are shown in Figure 11. It may be seen that the material has a mobility of zero at pH 5.3. This is the isoelectric point of influenza A virus. Some viruses seem to have maximum stability in the region of the isoelectric point. Partially complete studies indicate that this is not true for influenza virus. The question of influenza virus stability is being approached as a kinetic problem. Thus far, reasonably complete data have been obtained for the kinetics of the destruction of the red blood cell agglutinating factor (*24, 25*). As can be seen in Figure 12, when a solution of influenza A virus is heated, the reciprocal of the square root of red blood cell agglutinating activity is a linear function of time. This is an unexpected complication. One would anticipate that this destruction would be a first order reaction. Instead it seems to be a three-halves order reaction. This apparent order is probably not real, however, for a complicated kinetic mechanism such as this could result from inhomogeneity of the agglutinating factor with respect to rate of destruction. In any case the linear relationship between reciprocal of square root of concentration and time affords a convenient empirical method of determining the relative rates of the reaction under various conditions. A sort of reaction velocity constant can be calculated for the reaction by this means. Such velocity constants were determined in a variety of buffers at different temperatures. In Figure 13 the logarithms of the velocity constants are plotted against the reciprocals of the absolute temperature for several of the buffers. From these plots the reaction velocity constant at a particular temperature can be read off for each buffer. In Figure 14 the logarithm of the specific reaction velocity at 55°C. for the destruction of the hemagglutinin is plotted as a function of pH. It can be seen that the reaction has a minimum rate at pH 8.4. This means that the hemagglutinin has a maximum stability at 55°C. at pH 8.4, a value considerably higher than the isoelectric point.

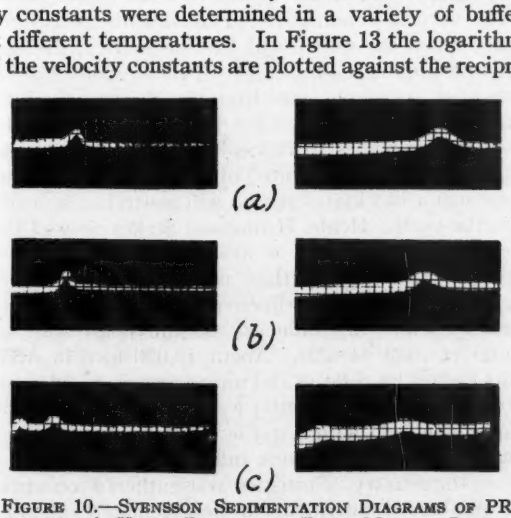

FIGURE 10.—SVENSSON SEDIMENTATION DIAGRAMS OF PR 8 INFLUENZA A VIRUS FRACTIONS. FROM MILLER, LAUFFER, AND STANLEY (*17*)

(*a*) Crude unfractionated virus, (*b*) heavy centrifuge fraction, (*c*) light centrifuge fraction.

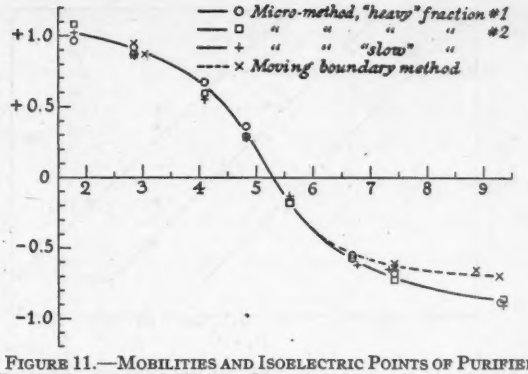

FIGURE 11.—MOBILITIES AND ISOELECTRIC POINTS OF PURIFIED PR 8 INFLUENZA A VIRUS PREPARATIONS. FROM MILLER, LAUFFER, AND STANLEY (*17*)

The abscissa scale represents pH, the ordinate represents mobility in cm. per sec. per volt per cm. × 10^4.

A previous study of some phases of the physical properties of influenza virus was carried out by Friedewald and Pickels (*26*) and a simultaneous study was carried out by Beard and associates (*27*). In all important respects the results of these studies are in accord with ours. These investigators studied not only the virus of influenza A, but also those of influenza B and swine influenza. The general conclusions regarding the natures of these viruses are similar to those described for influenza A virus.

Preliminary chemical analyses carried out by Knight indicate that influenza virus preparations are composed on a dry weight basis of about 70 per cent protein, 24 per cent lipoidal material, and 6 per cent carbohydrate (*23*). The figures for the water content obtained from viscosity and density measurements, 78 per cent and 60 per cent, are very much like those given for the water contents of many types of biological materials—yeast

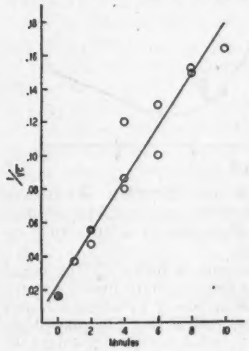

FIGURE 12.—THE COURSE OF DESTRUCTION AT 61°C. OF THE HEMAGGLUTININ OF PR 8 INFLUENZA A VIRUS IN A PHOSPHATE BUFFER OF IONIC STRENGTH 0.20 AND pH 6.9. FROM LAUFFER AND CARNELLY (*24*)

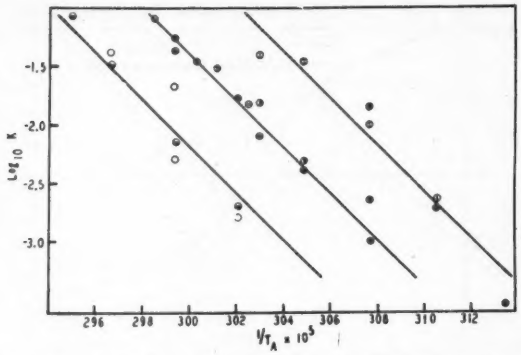

FIGURE 13.—THE LOGARITHM OF THE SPECIFIC REACTION VELOCITY FOR THE DESTRUCTION OF THE HEMAGGLUTININ OF PR 8 INFLUENZA A VIRUS PLOTTED AGAINST THE RECIPROCAL OF THE ABSOLUTE TEMPERATURE. FROM LAUFFER AND SCOTT (*25*)

◒ = Virus preparation No. 1 in phosphate buffer at pH 7.86; ○ = same at pH 7.59; ⊖ = same at pH 7.15; ⊙ = same at pH 6.47; ◐ = virus preparation No. 2 in ammonia buffer at pH 9.55; ● = same in phosphate buffer at pH 6.74; ⊗ = same in acetate buffer at pH 5.76.

and bacteria, for example. The ability of the influenza virus particle to lose large quantities of water osmotically indicates that this virus has either the structure of a gel or a semipermeable membrane like many living cells. When all of these facts are considered, it is obvious that these particles resemble small organisms more than large molecules.

The studies of Francis, Horsfall, Hirst, Henle, and others have shown that it is possible to vaccinate an individual against influenza. In general there are two processes of vaccination—the introduction of live virus, preferably of a mild strain, into the body by an unnatural route, and the introduction of a killed suspension of virus into the body. Vaccination against influenza is of the latter sort. Totally unpurified virus, such as that found in the allantoic fluid of influenza-diseased

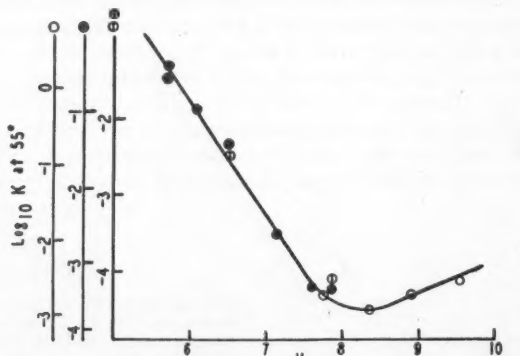

FIGURE 14.—THE LOGARITHM OF THE SPECIFIC REACTION VELOCITY AT 55°C. FOR THE DESTRUCTION OF THE HEMAGGLUTININ OF PR 8 INFLUENZA A VIRUS PLOTTED AS A FUNCTION OF pH. FROM LAUFFER AND SCOTT (*25*)

○ = virus preparation No. 2 in ammonia buffer (left vertical scale); ● = virus preparation No. 1 in phosphate buffer (center vertical scale); ⊗ = virus preparation No. 2 in acetate buffer (right vertical scale); ⊙ = virus preparation No. 2 in phosphate buffer (right vertical scale).

chicken embryos, can serve as a vaccine; however, the fundamental biological, chemical, and physical studies on the nature of influenza virus have led to methods of purifying and concentrating the virus subsequently converted into vaccine. This results in a product with higher antigenic power and with lower potentiality for inducing adverse physiological reactions.

During the war as a result of the biological studies on influenza virus carried out in several laboratories and of the physical and chemical studies carried out at the Rockefeller Institute, two kinds of influenza vaccine were developed. Each is now available for civilian use. Both vaccines consist of virus concentrated from the allantoic fluid of infected chicken embryos and treated with about one part per 10,000 of formaldehyde, an amount sufficient to destroy the infectivity but insufficient to destroy the antigenic power. A small amount of a bacteriostatic substance, such as phenyl mercuric nitrate, is often added. Each vaccine consists of a mixture of three strains of influenza virus—one fourth PR 8 influenza A, one fourth Weiss influenza A, and one half Lee influenza B. The two vaccines differ with respect to the method of concentration. The vaccine first accepted by the Army was concentrated by precipitation of the virus from cold allantoic fluid by means of chicken red blood cells, followed by elution of the virus at body temperature (*13*). About a tenfold concentration is possible by this method. The vaccine subsequently developed as an outgrowth of the physical and chemical studies just discussed is concentrated by means of the Sharples supercentrifuge (*14*). The formaldehyde and the bacteriostatic agent are added to the allantoic fluid before centrifugation. This method is capable of concentrating the inactivated virus somewhat more than the red-cell method, and it seems to give a product less contaminated with extraneous matter.

The vaccine is administered by subcutaneous injection. When the centrifugal vaccine is used, the dose recommended is 0.3 mg. (*28*). This is about half the virus that can be obtained from the allantoic fluid of a single infected embryo. An individual thus vaccinated develops antibodies to influenza virus. The presence of these can be demonstrated by the fact that the serum from such a vaccinated person will neutralize or inactivate the virus. Henle, Henle, and Stokes showed that vaccinated persons had a much higher resistance to experimental influenza than nonvaccinated ones (*5*). An extensive test of the effectiveness of vaccination was made by the Army Influenza Commission during the winter of 1943–44 (*29*). About 12,000 men in ASTP units located at colleges and universities in widely separated sections of the country were inoculated, half with vaccine and half with a sterile salt solution. Within a few weeks a fairly severe influenza epidemic spread across the country. Statistics were gathered concerning the numbers of individuals in the vaccinated and in the control groups that developed clinically recognizable influenza. Of the approximately 6000 vaccinated individuals, 2.22 per cent developed influenza, and of the

approximately 6000 controls, 7.11 per cent developed the disease. The ratio is better than three to one in favor of the vaccinated group. Hirst, Rickard, and Friedewald have shown that even a year after vaccination, the incidence of disease is still 35 per cent below that of unvaccinated individuals (*30*). In view of these favorable statistics it seems probable that the time when influenza can be numbered among the conquered diseases is near at hand.

The conquest of influenza, important as it is in terms of human welfare, has been a by-product of basic scientific studies directed principally toward discovering the nature of viruses in general and specifically toward discovering the nature of the influenza virus. The development of a suitable vaccine was, and the future development of even better vaccines will be, an inevitable result of an extension of knowledge of the influenza virus as an entity. The study of influenza virus was made possible by the pioneering work following the crystallization of tobacco mosaic virus. This feat was made possible by the experience amassed in the purification and crystallization of other biologically active proteins, particularly the enzymes. Yet who would ever have dreamed that the crystallization of urease and of pepsin opened the way to the conquest of influenza? Such things come under the heading of useless academic research. That being the case, it is hoped that the writer has succeeded in transmitting a little of his own enthusiasm for useless research.

LITERATURE CITED

(1) SHOPE, R. E., *Harvey Lectures*, **31**, 183 (1936); *Medicine*, **15**, 453 (1936).
(2) SMITH, W., C. H. ANDREWES, AND P. P. LAIDLAW, *Lancet 2*, **225**, 66 (1933).
(3) SMORODINTSEFF, A. A., M. D. TUSHINSKY, A. I. DROBYSHEVSKAYA, A. A. KOROVIN, AND A. I. OSETROFF, *Am. J. Med. Sci.*, **194**, 159 (1937).
(4) BURNET, F. M., AND M. FOLEY, *Med. J. Australia*, **2**, 655 (1940).
(5) HENLE, W., G. HENLE, AND J. STOKES, *J. Immunol.*, **46**, 163 (1943).
(6) FRANCIS, T., JR., *Bull. N. Y. Acad. Med.*, **17**, 268 (1941); *Harvey Lectures*, **37**, 69 (1941–42).
(7) ANDREWES, C. H., P. P. LAIDLAW, AND W. SMITH, *Lancet 2*, **227**, 859 (1934).
(8) WOODRUFF, A. M., AND E. W. GOODPASTURE, *Am. J. Path.*, **7**, 209 (1931).
(9) BURNET, F. M., *Brit. J. Exptl. Path.*, **17**, 282 (1936); *Australian J. Exptl. Biol. Med. Sci.*, **17**, 39 (1941).
(10) HIRST, G. K., *Science*, **94**, 22 (1941).
(11) MCCLELLAND, L., AND R. HARE, *Can. Pub. Health J.*, **32**, 530 (1941).
(12) HIRST, G. W., AND E. G. PICKELS, *J. Immunol.*, **45**, 273 (1942).
(13) FRANCIS, T., JR., AND J. E. SALK, *Science*, **96**, 499 (1942).
(14) STANLEY, W. M., *J. Exptl. Med.*, **81**, 193 (1945).
(15) LAUFFER, M. A., AND W. M. STANLEY, *ibid.*, **80**, 531 (1944).
(16) LAUFFER, M. A., AND G. L. MILLER, *ibid.*, **80**, 521 (1944).
(17) MILLER, G. L., M. A. LAUFFER, AND W. M. STANLEY, *ibid.*, **80**, 549 (1944).
(18) STANLEY, W. M., *ibid.*, **79**, 255 (1944); *ibid.*, **79**, 267 (1944).
(19) KNIGHT, C. A., *ibid.*, **83**, 11 (1946).
(20) WILLIAMS, R. C., AND R. W. G. WYCKOFF, *Proc. Soc. Exptl. Biol. Med.*, **58**, 265 (1945).
(21) SHARP, D. G., A. R. TAYLOR, I. W. MCLEAN, D. BEARD, AND J. W. BEARD, *Science*, **100**, 151 (1944); *J. Biol. Chem.*, **159**, 29 (1945).
(22) LAUFFER, M. A., *J. Am. Chem. Soc.*, **66**, 1195 (1944).
(23) KNIGHT, C. A., *J. Exptl. Med.*, **80**, 83 (1944).
(24) LAUFFER, M. A., AND H. L. CARNELLY, *Arch. Biochem.*, **8**, 265 (1945).
(25) LAUFFER, M. A., AND E. M. SCOTT, *ibid.*, **9**, 75 (1946).
(26) FRIEDEWALD, W. F., AND E. G. PICKELS, *Proc. Soc. Exptl. Biol. Med.*, **52**, 261 (1943); *J. Exptl. Med.*, **79**, 301 (1944).
(27) SHARP, D. G., A. R. TAYLOR, I. W. MCLEAN, D. BEARD, AND J. W. BEARD, *J. Biol. Chem.*, **156**, 585 (1944).
(28) STANLEY, W. M., *Chem. Eng. News*, **24**, 755 (1946).
(29) Army Influenza Commission, *J. Am. Med. Assoc.*, **124**, 982 (1944); *Am. J. Hyg.*, **42**, 1, 12, 21, 28, 45, 57, 94 (1945).
(30) HIRST, G. K., E. R. RICKARD, AND W. F. FRIEDEWALD, *J. Exptl. Med.*, **80**, 265 (1944).

Electropolishing Process for Silver

Silver has now joined the fast-growing group of metals receiving a brilliant luster by electrolytic treatment. This method is "electroplating in reverse." A current opposite in direction to that employed for ordinary plating removes metal preferentially from the high spots to produce a mirror-smooth surface. It replaces manual and mechanical buffing.

The process has been used for over a year for polishing plated silver tableware at Oneida, Ltd., where research on the subject has been carried on intensively since 1939. A patent will soon be issued to S. E. Eaton of Arthur D. Little, Inc., on an invention which has made possible substantial savings in the manpower required without electropolishing. Improvement in quality has also been noted, especially at sharp edges where mechanical buffing usually removes too much silver and in deep recesses which are inaccessible to the buffing wheel.

Electropolishing in general is a relatively new finishing procedure which has developed rapidly during the last ten years. The most important application so far has been the polishing of stainless steel, and several large installations have been operating with strong acidic baths for a number of years. Aluminum, zinc, copper, brass, nickel, tin, cobalt, nickel-silver, and various iron alloys can also be polished in acid baths. These baths usually require rather a high current density, which in commercial practice means expensive equipment. The acid is used up in the process.

The new silver process differs from earlier methods for other metals in its simplicity and economy. Its alkaline cyanide bath is much the same as for silver plating and does not require heating. Current density also is in the low plating range, and plants may thus use their regular equipment. Since electrical efficiencies are almost 100 per cent, power costs are very low, and silver is continually recovered from the bath, which thus has a long life. The new process can polish spoons, forks, knives, etc., on the same racks on which they are plated and is well suited to automatic operation. Time required for polishing depends on the condition of the surface, but is about five to twenty seconds; only a few per cent of the silver is removed, less than with mechanical buffing. The total cost is no more than for an equivalent amount of plating, and with tableware this has proved to be less than that of mechanical buffing

The development was stimulated by observation at Oneida that some electrodes in a silver bath occasionally appear to be polished. This had been known in the trade for some time, but no commercial applications were possible because of poor reproducibility. By the new process reproducibility is assured. Metals other than silver, for example cadmium, may be similarly polished using the new technique, but commercial application requires further development. In view of the cost reduction and quality improvement possible with this process, its applicability to a generous share of all silverware production (a sixty-million-dollar industry) seems assured.—Reprinted from the *Industrial Bulletin* of Arthur D. Little, Inc. (July, 1946).

The Fractionation of Isotopes

A. M. SQUIRES

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This is the fourth of a series of articles, written by Oak Ridge scientists, on the chemical significance of modern nuclear science and technology.

BEFORE the war significant amounts of several rare isotopes were concentrated by fractionation, and microgram lots of a great many isotopes were prepared nearly pure by the mass spectrograph. During the war fractionation of industrial quantities of U^{235} and deuterium and of semiworks amounts of C^{13} and N^{15} was accomplished. Industrial separation of U^{235} by mass spectrographs was successful. Large-scale enrichment of other isotopes will undoubtedly be undertaken in the future.

Concentrated isotopes are useful in chemical research. Small quantities of relatively pure isotopes are of importance in nuclear research. In addition to U^{235}, Pu^{239}, and H^2 large amounts of certain other isotopes having special nuclear properties may become of importance in nuclear engineering.

FRACTIONATION

The process of fractionation is best explained by an example. If a little benzene and toluene are shaken together in a closed container, it will be found, as soon as equilibrium is established, that the vapor phase has a higher relative concentration of benzene than exists in the liquid. This is a consequence of the higher vapor pressure of benzene, which is a reflection of its lower boiling point. It is convenient to describe this state of affairs by the following equation:

$$\alpha = \frac{n_1'/n_2'}{n_1/n_2}$$

where n_1 and n_2 are the numbers of molecules of benzene and toluene, respectively, per mol of liquid; n_1' and n_2' are the numbers per mol of vapor; and the symbol α, which is defined by the equation, is called the "relative volatility" of benzene with respect to toluene. The ratio n_1/n_2 is called the "abundance" of benzene in the mixture.

Now if one removes a little vapor and a little liquid from the container, one obtains two mixtures, one richer and one leaner in benzene than that originally introduced into the container. In general, if one wishes to separate the two components, the two new mixtures thus obtained are not pure enough. Each of them may be separated again into a vapor and liquid phase; and by repeating the process many times, practically pure benzene and toluene may be secured. In order that the products will contain more than a minute fraction of the original mixture and that nothing will be wasted, the process of recycling is used. After the original liquid fraction is separated into a liquid and vapor phase, vapor is returned to the first container to be mixed with the liquid resulting from the separation of the first vapor fraction. At every step of the separation process the vapor fraction is returned to the step above, and the liquid fraction is sent to the step below.

A fractionating column is a device for carrying out this process continuously. A stream of liquid descends through the column over plates or packing and becomes progressively richer in the less volatile component by exchange of molecules with a rising stream of vapor. Feed material is continuously introduced at an intermediate point in the column, and products are continuously removed at the two ends. A given molecule goes through a great many cycles of condensation and re-evaporation before finally emerging in one of the products.

Fractionation, then, is a process which multiplies a separation effect (in the above example, the difference in volatility between benzene and toluene) by setting up a sequence of separation steps, between which partially separated fractions are recycled. In principle any separation effect may be exploited in a fractionation device.

SEPARATION EFFECTS AVAILABLE FOR ISOTOPE FRACTIONATION

Four separation effects have been used for isotope fractionation—centrifugation, thermal diffusion, chemical exchange, and gaseous diffusion.[1] The last will be discussed most fully because it is the one with which the author is most familiar.

1. Centrifugation: If a mixture of two gases of differing molecular weights is placed in a centrifuge, a small concentration gradient establishes itself between the axis and periphery of the bowl because of the greater centrifugal force on the heavier molecular species. The ultimate gradient is the resultant of the centrifugal force effect and the opposing diffusion effect, *i. e.*, wherever a concentration gradient has been established, diffusion of the two molecular species tends to destroy the gradient.

Fractionation is accomplished by establishing a downward current of gas at the periphery of the centrifuge bowl and an upward current along the axis. The upward current grows richer in the lighter molecules by exchange between the axis and the periphery. The equipment and flow rates are designed so that an indi-

[1] For the enrichment of deuterium ordinary distillation and electrolysis have been used.

vidual molecule passes back and forth between the two currents a great many times before finally emerging from one of the ends of the bowl—that is to say, on the average a given molecule travels a little way along the periphery, diffuses over to the axis, a little way along the axis in the opposite direction, and back to the periphery. Thus the recycling does not consist of well-defined streams but results from the average of a great many molecular paths.

Centrifugation has been successfully used on a pilot plant scale to produce a slight enrichment of $U^{235}F_6$.

2. Thermal Diffusion: If a gas or liquid mixture is placed in a container, one wall of which is hot and the other cold, in many cases a small concentration gradient is established between the hot and cold wall. In the case of gas mixtures the lighter molecules tend to the hot wall, and the degree of separation can be predicted theoretically. The effect is greatest for the noble gases, whose molecules are like hard spheres, with short-range repulsive forces (decreasing as a very large power of the inverse of the distance between molecules). The effect disappears for soft molecules with repulsive forces varying as the inverse fifth power of the distance. Analysis of the phenomenon in the case of liquid mixtures is extremely complicated, and the separation effect is unpredictable.

Fractionation is achieved by vertical mounting of a two-walled column (*e. g.*, concentric cylinders) with a temperature gradient between the walls. Since the gas or liquid near the cold wall is denser, the action of gravity sets up convectional currents down the cold wall and up the hot wall. The spacing between the two walls is made very small so that a given molecule passes back and forth between the two currents a great many times before arriving at an end of the column.

Thermal diffusion was used during the war on a plant scale to effect a small enrichment of $U^{235}F_6$ in liquid UF_6 and to concentrate C^{13}.

3. Chemical Exchange: If ammonia gas and a solution of ammonium sulfate are placed in a closed container, it will be found that an exchange takes place between $N^{15}H_3$ in the vapor phase and the $(N^{14}H_4)$ ions in the liquid. At equilibrium the abundance of N^{15} in the vapor phase is about two per cent less than in the liquid. Similar exchange reactions have been found for a number of other isotopes (*e. g.*, deuterium, oxygen, sulfur), the likelihood of their existence being greater the smaller the atomic weight.

Appreciable enrichment is achieved in a fractionating column, in which a rising stream of ammonia vapor exchanges with a downflow of ammonium sulfate solution.

4. Gaseous Diffusion: The huge K-25 gaseous diffusion plant at Oak Ridge makes use of the principle of molecular diffusion (more properly "effusion") through very small holes for enrichment of U^{235} from the naturally occurring concentration of 0.7 per cent to concentrations many times as great.

T. Graham discovered in 1829 that different gases effuse from a high- to a low-pressure region at rates inversely proportional to the square roots of their molecular weights when the effusion occurs through holes sufficiently small. This results from the following facts:

(1) Suppose a small hole exists in a wall separating a high- and a low-pressure region. The number of gas molecules entering the hole in unit time from either region is proportional to the pressure in the region and to the average velocity of the molecules, provided the hole is so small that almost invariably the gas molecules enter the hole singly rather than a great many at once. The molecular velocity is the same in both regions, and so the rate of transfer from the high- to low-pressure region is proportional to the pressure difference.

(2) The average molecular velocities of different gases are inversely proportional to the square roots of their molecular weights since the average kinetic energy of all gas molecules is the same at a given temperature. Kinetic energy = $\frac{1}{2}$(Molecular Weight)-(Molecular Velocity)^2.

If a mixture of two gases is allowed to effuse through a small hole from a high-pressure region to a region of zero pressure, a separation will be expected. If each of the two gases effuses as if the other were not present (*i. e.*, at a rate proportional to its partial pressure and to the inverse of the square root of its molecular weight), the separation will be given by

$$\alpha^0 = \sqrt{M_2/M_1} = \frac{n_1'/n_2'}{n_1/n_2}$$

where M_1 and M_2 are the molecular weights of the light and heavy species; n_1' and n_2' are the numbers of molecules of light and heavy per mol in the first small amount of effused gas; n_1 and n_2 are the numbers per mol in high-pressure gas before any effusion has occurred; and α^0 is the ideal separation factor (analogous to relative volatility in distillation).

Actually, such ideal effusion never occurs. Since the low pressure can never be zero, some back diffusion from the low-pressure to the high-pressure region occurs with separation in the opposite direction of the main effusional flow. More important is the fact that two different gases never actually effuse independently of one another. Even if it is seldom that more than one molecule enters the hole at a given instant, collisions between molecules occur while they are passing through the hole. The effect of this molecular jostling is to speed up the slower, heavier molecules and to slow down the faster, lighter molecules, thus bringing their effusion rates closer together and reducing the separation effect. This inefficiency is greater the higher the pressure, since the number of intermolecular collisions is proportional to the pressure. Still another inefficiency results from the existence of a small amount of nonseparating viscous flow (proportional to the difference of the squares of the pressure) through a hole however small.

The diffusion barrier is a porous sheet material containing myriads of holes a few millionths of a centimeter in diameter. It is characterized by specifying two quantities: permeability and separation factor. Permeability, γ, is defined as the fraction of the number of molecules striking the surface of the barrier which ef-

fuse. The separation factor, α, decreases with increasing permeability if the number of pores is held constant. The separation factor decreases with increasing ratio of back pressure to fore pressure (because of back diffusion) and with increasing fore pressure (because of greater number of intermolecular collisions within the barrier pores).

Separation is carried out continuously in a diffusion stage. In a K-25 diffusion stage a centrifugal blower pumps UF_6 gas into a diffuser containing a large number of square feet of barrier. Half the gas diffuses through the barrier into a low-pressure region and is enriched in $U^{235}F_6$. It is carried away from the stage by a second centrifugal blower which maintains the low-pressure region. The other half remains undiffused and is depleted in $U^{235}F_6$. Because of the combined effect of the enrichment of the diffused gas and the depletion of the undiffused gas, the over-all difference in $U^{235}F_6$ concentration between the two streams leaving the diffuser is about 40 per cent greater than the difference between the concentration in a small amount of diffused gas and the high-pressure stream from which the small amount has just diffused. The latter difference is somewhat smaller than that calculated from the barrier's separation factor, because inefficient mixing of the high-pressure stream results in a stagnant layer of gas adjacent to the barrier which is somewhat leaner in $U^{235}F_6$ than the main stream. This inefficiency is reduced to a minimum by proper design of the channel for the high-pressure stream.

The ideal separation factor of $U^{235}F_6$ versus $U^{238}F_6$ is $\sqrt{352/349}$ or 1.0043. It is clear that a given molecule of $U^{235}F_6$ must undergo diffusion a great many times before it finds itself in a mixture appreciably richer in $U^{235}F_6$. The diffusion stages are arranged in a cascade. The diffused gas from a stage is advanced to be fed to the next richer stage; the undiffused gas flows through a valve, which controls the pressure in the stage, and is fed to the next leaner stage. The K-25 cascade consists of several thousand such stages. It is fed continuously at an intermediate stage with UF_6 prepared from naturally occurring uranium; a waste stream depleted in U^{235} is removed at the bottom; and a product stream appreciably enriched in U^{235} is removed at the top. Between any two stages above the feed point there is a small net forward flow of UF_6 corresponding to the product rate. There is also a net forward flow of $U^{235}F_6$ corresponding to that contained in the product. At a given stage the net flow of $U^{235}F_6$ results partly from the $U^{235}F_6$ occurring in the net forward flow of UF_6 gas and partly from the product of the interstage flow rate times the difference in concentration between the interstage streams. At the feed point this difference is very small, and the amount of $U^{235}F_6$ in the net forward flow of UF_6 is only 0.7 per cent, and so interstage flow rates tens of thousands of times the product rate are required. Higher up in the cascade the amount of $U^{235}F_6$ in the UF_6 net forward flow increases, and the difference in concentration between the interstage streams becomes greater, and so smaller interstage flow rates are required.

In the K-25 plant an average $U^{235}F_6$ molecule undergoes diffusion about 2,000,000 times before emerging in the product stream.

In design of the K-25 plant choices had to be made of the following independent variables: (1) Barrier permeability (if high, less barrier area and smaller stages, but poorer separation and hence more stages). (2) Operating fore pressure (same as 1). (3) Back to fore pressure ratio (if low, separation better and fewer stages, but higher pumping costs). (4) Stage size, *i. e.*, interstage flow rate (if large, only a small concentration difference between interstage streams is required, and so the difference between the concentrations of two adjacent stages is larger than if small stages are used; hence, the choice is between a few large stages and a greater number of small stages).

An important dependent variable is the plant's inventory of $U^{235}F_6$, which is many times the daily product take-off of $U^{235}F_6$ in spite of care in design to minimize all equipment volumes. A characteristic of isotope fractionation devices working with a small separation effect to produce a large enrichment is a long start-up time, during which the plant extracts its own steady-state inventory from feed, before material of the desired product concentration can be withdrawn.

One can imagine a plant in which each stage is designed with the best value of each of the above variables. In such a plant the stage size, pressures, etc., would vary continuously from stage to stage. No two pieces of equipment would be alike. Large stages and high operating pressures would be preferred near the feed point, small stages and low pressures near the top. In practice it is necessary to settle on a few standard stage designs, for ease of fabrication, construction, and operation, but with some loss of plant efficiency.

Some other problems are worth noting. Methods were developed for predicting the output of the K-25 plant at product rates other than design and under all possible operating conditions. In this way all possible steady-states of the plant could be examined when production schedules were drawn up, and the best selected for actual use in operation. In addition, theoretical studies were made of the time-dependent behavior of the plant so that the time required to go from one steady-state to another could be allowed for in production scheduling. The hydrodynamic control of the cascade was studied theoretically, and the response characteristics of the control valves specified so that pressure waves through the plant are damped and do not grow dangerously. Since the K-25 plant operates below atmospheric pressures, contaminants leak continuously into the process stream. In the case of a serious break large amounts can enter the plant in a short space of time. The behavior of contaminants in the process stream was studied theoretically, and equipment was developed for their detection and removal.

The K-25 plant development required marvels of chemical and physical research and mechanical engineering, mainly growing out of the highly corrosive character of UF_6 gas and the necessity of operating at re-

duced pressures. The diffusion barrier itself met fantastic requirements. Its pores must not exceed a few millionths of a centimeter, yet not plug up during operating with products of corrosion by UF_6; and the sheet material must be mechanically strong to permit fabrication into diffuser units. For a description of some of the engineering and construction problems, see references (*2*), (*3*), and (*4*).

In an article of this length no attempt could be made to give just credit to the many men in the team of scientists and engineers who worked on the gaseous diffusion project. In spite of the unfairness to others, the author cannot resist mention of three men—P. C. Keith, John Dunning, and Manson Benedict—who combined the qualities of daring and judgment, optimism in the face of seeming failure, and unerring analysis, caution, and thorough attention to detail, which had no small part in the unqualified success of the K-25 development.

CHOICE OF SEPARATION METHOD

The choice of a separation method depends on many factors beyond the scope of this article. Some of the advantages and disadvantages of the various methods are noted:

1. Electromagnetic Separation: The mass spectrometer will be preferred where relatively small amounts of very pure isotopes are required. A single machine may be used to concentrate a number of different isotopes in succession without extensive modification of equipment.

2. Fractionation: All fractionation methods depend on availability of a suitable working gas or liquid, and in the case of thermal diffusion and chemical exchange, the discovery of a separation effect. None of the fractionation methods is particularly suited to making small amounts of very pure isotopes because of the larger number of fractionation steps required. Fractionation is particularly well suited, however, to production of large amounts of slightly enriched isotopes, which are adequate for many research purposes. When large amounts of highly enriched isotopes are required, fractionation will probably be preferred to the electromagnetic method. In general, large capacity is achieved more readily in the case of chemical exchange and gaseous diffusion methods than in the cases of thermal diffusion and centrifugation. The size of the column or stage of the former methods is almost unlimited, while the size of a centrifuge is limited by mechanical considerations, and that of a thermal diffusion column by the very small spacing allowed.

LITERATURE CITED

(1) UREY, H. C., *J. Applied Phys.*, **12**, 270 (1941).
(2) SMYTH, H. W., "Atomic Energy for Military Purposes," Princeton University Press, Princeton, **1945**.
(3) KEITH, P. C., *Chem. Met. Eng.*, **53**, No. 2, 112 (1946).
(4) HOGERTON, J. F., *Eng. News-Record*, December 13, **1945**, p. 134.

"You've probably heard of pennies from heaven," our metallurgist friend remarked the other day, "but it was nickel, not copper, that really came to us from that direction." "Sounds like dangerous inflation," we commented, but he merely glared. "The sword-blades of ancient China and Persia became famous because of their strength, keenness, and resistance to rust. The reason was that they were made of fused iron and nickel, which literally had fallen out of the sky, in the form of meteorites. Only recently have men learned to imitate and improve on this dramatic gift of nickel from heaven. Stainless steel, for example, is a modern wonder-metal made possible by the use of nickel as an alloy." "Oh," we exclaimed with a bit of disappointment, "then the Old Nick didn't have anything to do with nickel after all." "Well," the metallurgist conceded, "the Germans who discovered nickel deposits in Saxony thought he did. In disgust, they dubbed the metal 'kupfernickel,' meaning 'copperdevil,' because they were after copper and the admixture of the whitish metal annoyed them no end. The Chinese, however, were so eager to obtain nickel for the purpose of mixing it with copper and zinc, that they imported it from Litchfield County, Connecticut, even before the American Revolution. The Chinese made a metal compound which they called 'paktong' and which they shipped to Europe where a Swedish scientist, Engstrom, finally succeeded in imitating it. The Germans, who had scorned the obviously non-Aryan mixture in their own mines, now seized upon paktong and because it had a silvery appearance made and sold a variety of utensils from it. That is how we obtained German silver, which is neither silver nor German. Just to make the geography quite clear to you, the present world nickel supply comes principally from Canada, where it was developed by American promoters. By far the greatest tonnage of nickel goes into the making of alloy steels."—Steelways (July, 1946).

INORGANIC NITROSYL COMPOUNDS

II.—Coordination Compounds

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INTRODUCTION

IN A previous communication (*57*) the possible roles which the nitrosyl grouping might play in the formation of inorganic compounds and a number of simple cationic and anionic derivatives were discussed. In addition to these compounds there are many known substances in which the nitrosyl group is directly associated with metal atoms or ions (*4, 15, 59, 76, 77, 79, 81*). The structures of many of these materials have been only incompletely elucidated, but it appears that such compounds cannot be regarded as derivatives of hyponitrous acid, $H_2N_2O_2$. Thus, such nitrosyls are not obtained in reactions involving hyponitrites, do not contain the doubled NO group characteristic of hyponitrites, and liberate nitric oxide rather than nitrous oxide upon treatment with acids (*76, 77, 79*). The remaining structural possibilities all involve coordination, so these compounds may in a general sense be regarded as coordination compounds.

STRUCTURAL CONSIDERATIONS

As previously indicated (*57*) the nitrosyl group might coordinate as a neutral molecule, as an NO^- ion after gaining an electron, or as an NO^+ ion after losing an electron. To these one might add the possibility of bonding to the metal through four electrons (*4, 62, 76*). These structural possibilities have all been examined rather carefully (*75, 76*). Before they can be considered in detail, however, it is necessary to point out that regardless of the nature of the coordinating nitrosyl group the nitrogen functions as the donor. This is indicated by the fact that reduction of a complex, such as $[Fe(CN)_5(NO)]^=$, yields an ammine, $[Fe(CN)_5(NH_3)]^=$, whereas treatment of the same nitrosyl complex with alkali converts it to a nitro complex, $[Fe(CN)_5(NO_2)]^{\equiv}$ (*15, 77*).

The existence of volatile nitrosyl carbonyl compounds, such as $Fe(NO)_2(CO)_2$ and $Co(NO)(CO)_3$, and the similarities between these compounds and the corresponding metal carbonyls suggest coordination of neutral nitric oxide molecules. Such a condition would assume attachment of these groups through electron-pair bonds and would preserve the odd-electron character of the original nitric oxide. This would impart paramagnetic properties to the nitrosyl carbonyls. They are, however, diamagnetic (*64, 76*). Furthermore, if neutral nitric oxide molecules were involved, they should be replaceable by other neutral molecules without alteration in compound type (*76, 77*). Actually, treatment of nitrosyl carbonyls with such materials as pyridine and orthophenanthroline replaces carbonyl groups, not nitrosyl groups (*24*). In addition, replacement of the neutral carbonyl group by the nitrosyl group alters the oxidation state in complex ions, *e. g.*, $[Fe(CN)_5(CO)]^=$ goes to $[Fe(CN)_5(NO)]^=$, an alteration which could not be effected by a neutral group (*77*). Experimental evidences indicate coordination of neutral nitrosyl groups to be very unlikely.

Evidence for the coordination of negative nitrosyl radicals is also unconvincing. If the nitrosyl group were to add in this fashion, it would function somewhat like a halide ion. The properties of most nitrosyl coordination compounds are not consistent with such character (*76*). Only in the case of the unusual pink compounds containing the ion $[Co(NH_3)_5(NO)]^{++}$ does there appear to be any very definite evidence for the existence of a coordinated NO^- ion (*55*). The diamagnetic properties of this ion suggest the presence of trivalent cobalt, formed from the cobaltous ion by transfer of an electron to nitric oxide (*55*). The resulting NO^- ion might then function in the same fashion as the Cl^- ion in the $[Co(NH_3)_5Cl]^{++}$ ion. Thus, the nitrosyl- and chloropentammine cobaltic salts should be, and actually are, comparable in character (*55, 77*). It seems not unlikely that the diamagnetic ruthenium compounds yielding the ions $[Ru(NH_3)_4(H_2O)(NO)]^{+++}$ and $[Ru(NH_3)_4Cl(NO)]^{++}$ may also contain coordinated NO^- groups (*55*). In this respect an analogy to diamagnetic sodium nitrosyl is apparent (*84*). The suggestion (*55*) that the nitrosyl grouping may be negative in cationic complexes and positive in anionic complexes appears to have some merit.

Coordination as a positive group appears somewhat more likely in most instances (*4, 64, 76, 77*). The existence of such a radical is well recognized (*57*) as is also its triple bond character

$$:N:::O:^+ \quad \text{or} \quad :N{\equiv}O:^+$$

The nitrosyl cation is, therefore, isosteric with the carbon monoxide molecule and the cyanide ion, the structures of which are

$$:C:::O: \quad \text{and} \quad :C:::N:^-$$

On this basis, certain similarities among nitrosyl, carbonyl, and cyano complexes would be expected if the nitrosyl bore a positive charge (*77*). That such similarities do exist is indicated by the modes of formation and the formulas summarized in Table 1 (*77*) and by the similarities apparent in the properties of these compounds.

Acceptance of the concept of coordination by the NO^+ radical is contingent upon a satisfactory explana-

TABLE 1

COMPARISONS AMONG COORDINATION COMPOUNDS

	Cyano derivatives	*Carbonyl derivatives*	*Nitrosyl derivatives*
Coordinating group	:C:::N:$^-$	:C:::O:	:N:::O:$^+$
Linkage	M ← C ≡ N	M ← C ≡ O	M ← N ≡ O
Examples	$K_3[Mn(CN)_6]$ $K_4[Fe(CN)_6]$ $K_4[Ru(CN)_6]$	$K_3[Fe(CN)_5(CO)]$	$K_3[Mn(CN)_5(NO)]$ $K_2[Fe(CN)_5(NO)]$ $K_2[Ru(CN)_5(NO)]$

tion of the oxidation states found among these complex materials. Since the formation of a cation from nitric oxide necessitates the loss of a single electron, it is not unreasonable to assume transfer of this electron to the acceptor metal atom or ion. As a result, that material must undergo reduction with a decrease of one unit in oxidation state. That this is apparently the case is well illustrated by the nitroprussides, $M_2^I[Fe(CN)_5(NO)]$. The relative stabilities of the nitroprussides as compared with the instabilities of the pentacyano ferric complexes, $[Fe(CN)_5A]^-$ (A = H_2O, NH_3), plus their diamagnetic properties, indicate that they contain ferrous iron (*15*, *55*, *76*, *77*). This is further indicated by their conversion by alkali to nitro ferrous complexes, $M_4^I[Fe(CN)_5NO_2]$ (*15*). It appears, therefore, that the ferrous state is maintained in the nitroprussides by transfer of an electron from the nitrosyl group. The over-all -2 oxidation state of the complex ion is then apparent from the inclusion of the NO^+ radical. On this basis the marked similarities among the ions, $[Fe(CN)_5(NO)]^=$, $[Fe(CN)_5(CO)]^=$, and $[Fe(CN)_6]^{=\!=}$, is readily apparent, as is also the alteration in over-all oxidation state in the series. Comparable analogies exist between the monovalent manganese derivatives, $[Mn(CN)_5(NO)]^=$ and $[Mn(CN)_6]^{-5}$, between the divalent ruthenium derivatives, $[Ru(CN)_5(NO)]^-$ and $[Ru(CN)_6]^{=\!=}$, and between the divalent osmium derivatives, $[OsCl_5(NO)]^-$ and $[OsCl_6]^{=\!=}$(*77*).

Agreement between the effective atomic numbers of the central elements in many nitrosyl derivatives and the atomic numbers of inert gas elements gives further indication that attachment of the nitrosyl group involves three electrons (*4*, *77*). Thus, the effective atomic numbers of iron and manganese are 36 in the complex materials listed in Table 1, while the effective atomic number of ruthenium in the listed ruthenium compounds is 54. The same is true in the nitrosyl carbonyl compounds and their derivatives (*77*). In fact, Sidgwick and Bailey (*77*) have proposed this inert gas rule as a general criterion for nitrosyl compounds and have extended to many and varied examples their relation

$$G - \frac{xm + 2y + 3z}{x} = x - 1$$

where G is the atomic number of the next inert gas, x the number of atoms of the metal M of atomic number m in compounds of the type $M_x(CO)_y(NO)_z$, y the number of mols of CO or other similar group, and z the number of mols of NO. Indeed, it appears that contribution of three electrons binds the nitrosyl group more firmly than the carbonyl (*60*).

While this concept of bonding is eminently successful in accounting for the compositions of most nitrosyl compounds, it does introduce certain inconsistencies. Donation of an electron pair to a metallic atom or ion by nitrogen in the NO^+ group must of necessity impart a negative charge to that metallic material. The structure

$$\bar{M}:\overset{+}{N}:::\overset{+}{O}:$$

would then characterize each bond (*77*). As Pauling points out (*62*), the accumulation of such a negative charge upon a metallic material is unlikely. An alternative structure for the cyano and carbonyl derivatives which eliminates such a charge accumulation assumes the presence of four bonding electrons between the metal and carbon (*62*), the coordinating group having accepted an electron pair from the metal atom or ion. An extension of this concept to the nitrosyl compounds is not improbable, and the contribution of the linkage

$$M::\overset{+}{N}::\ddot{O}:$$

may be a major one in such materials (*62*).

The possibility of bonding through four electrons was ruled out by Sidgwick and Bailey (*77*) as violating the rules of maximum coordination; however, their concept of such a bond involved contribution of all four electrons by nitrogen. Seel (*76*), while admitting that such a bond would account for the physical and chemical properties of the nitrosyls, opposed it from the theoretical point of view. Blanchard (*4*) recorded the structure as an alternative to the electron pair bond structure but offered no serious support for it. Gelman (*21*), on the other hand, suggested that nitric oxide, together with ethylene and carbon monoxide, behaves first as a donor to platinum and then as an acceptor, with the ultimate transfer of one electron to the platinum and the sharing of four electrons between the platinum and nitrogen. The marked *trans* influence of the nitrosyl grouping in such compounds and the analogy between materials such as $[Pt(NO)Cl_3]^-$ and $[Pt(C_2H_4)Cl_3]^-$ are cited in support of such a linkage (*21*, *22*).

In many respects a four-electron bond, as a partial or complete explanation of the linkage, is to be preferred to the electron-pair bond. Ultimate decision as to the correctness of either concept must await evaluation of M—N bond distances in numerous nitrosyl compounds of various types. It is apparent that a four-electron bond formed through combined donor and acceptor properties of the metal atom or ion will produce the same alteration in effective atomic number as an electron-pair bond formed by a donor nitrogen.

COMPOUNDS CONTAINING COORDINATED NITROSYL GROUPS

A considerable complexity among such compounds is apparent at first examination; however, many of these materials fall into several rather well-defined classes.

The discussion which follows is based upon one such method of classification.

A. The Nitrosyl Carbonyls and Related Compounds: The only nitrosyl carbonyls which have been definitely identified are those of cobalt and iron. The cobalt compound, $Co(NO)(CO)_3$, was first obtained by Mond and Wallis (*58*) by direct reaction of dry nitric oxide with cobalt tetracarbonyl, $[Co(CO)_4]_2$, but it can also be prepared by treating alkaline suspensions of cobaltous cyanide with carbon monoxide, followed by saturation with nitric oxide either with or without acidification (*5, 7, 8*). The second method is presumed to involve reaction of nitric oxide with cobalt carbonyl hydride, $HCo(CO)_4$, or its alkali derivatives (*5*), and yields the nitrosyl carbonyl as a yellow gas which condenses to a red liquid. A suspension of cobaltous hydroxide containing cysteine may be substituted for the cyanide (*14*), and treatment of active cobalt on pumice with carbon monoxide and nitric oxide also yields the nitrosyl compound (*7*). The iron compound, $Fe(NO)_2(CO)_2$, has been obtained, mixed with iron pentacarbonyl, by reaction of dry nitric oxide with iron tetracarbonyl, $[Fe(CO)_4]_3$ (*1*).

If the view that each nitrosyl group contributes three electrons to the metal be accepted, it is apparent that the iron and cobalt nitrosyl carbonyls form a graded series of compounds with nickel carbonyl, in which substitution of a nitrosyl group for a carbonyl accompanies each decrease in atomic number of the metal (*1, 15, 64*). Extension of this view would lead to the series $Ni(CO)_4$, $Co(NO)(CO)_3$, $Fe(NO)_2(CO)_2$, $Mn(NO)_3(CO)$, $Cr(NO)_4$, each member of which would contain a metal with an effective atomic number of 36 (*1*). Although the last two members of this series have not been isolated, the concept is a useful one. Inasmuch as the nitrosyl group is somewhat more polar than the carbonyl, it is not surprising that the increases in boiling and melting points given among the comparative properties listed in Table 2 (*1, 15*) should characterize the series.

Further indications of similarities among these compounds are apparent from electron diffraction data (*8*). All three compounds are tetrahedral, but the observed M—C and M—N bond distances (Table 3) are slightly less than those calculated from the sums of the covalent radii (*8*). This and the fact that the observed N—O bond distances are less than the calculated double bond distances suggest that the M—C and M—N bondings are similar and that both two-electron and four-electron bondings are important.

TABLE 2

COMPARISON OF PHYSICAL CONSTANTS

Property	$Ni(CO)_4$	$Co(NO)(CO)_3$	$Fe(NO)_2(CO)_2$
Molecular weight	170.73	172.98	171.89
Melting point, °C.	−23	−1.1	18.4
Boiling point, °C.	43	48.6	110 (extrap.)
Density at 20°C., g./ml.	1.31	1.47	1.56
Parachor	255.3	249.8	252.5
$\chi_{mol} \times 10^6$	−82	−46	...

TABLE 3

BOND DISTANCES FROM ELECTRON DIFFRACTION DATA

Bond	$Ni(CO)_4$	$Co(NO)(CO)_3$	$Fe(NO)_2(CO)_2$
M—C, A.U.	1.82 ± 0.02	1.83 ± 0.02	1.84 ± 0.02
C—O, A.U.	1.15 ± 0.03	1.14 ± 0.03	1.15 ± 0.03
M—N, A.U.		1.76 ± 0.03	1.77 ± 0.02
N—O, A.U.		1.10 ± 0.04	1.12 ± 0.03

Inasmuch as treatment of iron nitrosyl carbonyl with pyridine (*pyr*) and orthophenanthroline (*ophen*) produces, respectively, $Fe_2(NO)_4(pyr)_3$ and $Fe(NO)_2(ophen)$, and treatment of cobalt nitrosyl carbonyl in like fashion gives, respectively, $Co_2(NO)_2(CO)(pyr)_2$ and $Co(NO)(CO)(ophen)$ (*24*), it is evident that the nitrosyl group is more firmly attached than the carbonyl. This is further suggested by the formation of $Fe(NO)_2I$ from the iron compound and iodine (*24*). Further analogies with nickel carbonyl are apparent in the formation of $Ni(CO)_2(ophen)$ and $Ni_2(CO)_3(pyr)$ (*2*).

Closely allied with the nitrosyl carbonyls are the metal nitrosyls. Manchot and Enk (*40*) have reported the preparation of a black crystalline iron tetranitrosyl, $Fe(NO)_4$, by the reaction of nitric oxide with iron pentacarbonyl under pressure. This very reactive material was transformed into $Fe(NO)_3NH_3$ by liquid ammonia, into $Fe(NO)SO_4$ by dilute sulfuric acid, into $K[Fe(NO)_2S_2O_3]$ by potassium thiosulfate, into $K[Fe_4(NO)_7S_3]$ by potassium acid sulfide, into $Fe(NO)_2SC_2H_5$ by ethyl mercaptan, etc. No adequate structural picture has been advanced for iron tetranitrosyl, but it has been suggested (*15*) that the compound is perhaps a nitrosyl hyponitrite, $Fe(NO)_2N_2O_2$.

Although by analogy to iron the formation of a nitrosyl carbonyl upon treatment of ruthenium enneacarbonyl, $Ru_2(CO)_9$, with nitric oxide might be expected, Manchot and Manchot obtained ruthenium tetranitrosyl, $Ru(NO)_4$, at around 100°C. and red, crystalline ruthenium pentanitrosyl, $Ru(NO)_4$, at around 100°C. and red, crystalline ruthenium pentanitrosyl, $Ru(NO)_5$, at higher temperatures and under pressure (*50*). The existence of such nitrosyls has been questioned (*15*).

B. Nitrosyl Compounds of the Type $M^I(NO)_xA_y$: A number of nitrosyl derivatives of apparently monovalent metals have been described. These can be conveniently classified as follows:

1. Metal nitrosyl hydroxides: In the presence of methanol, iron pentacarbonyl and nitric oxide react to form a black, unstable material formulated variously as $Fe(NO)\cdot nCH_3OH$ (*43*) and $Fe_2(NO)_2(OCH_3)_2OH$ (*66*), but little is known about this substance.

More information is available concerning the reaction of nitric oxide with nickel carbonyl. In the presence of a trace of moisture and in the presence or absence of an inert solvent, this reaction yields a small amount of a water-soluble, basic, blue compound, Ni(NO)OH (*2, 15*). The reducing power of this material suggests the presence of monovalent nickel. In the presence of alcohols, this reaction yields larger quantities of alcohol-containing products. The methanol derivative has been formulated as $Ni(NO)(OCH_3)(OH)\cdot CH_3OH$ (*65, 66*) and as either $Ni(NO)OH\cdot 2CH_3OH$ or $Ni(NO)(OCH_3)\cdot CH_3OH\cdot H_2O$ (*2*), the latter formulations being the more probable in light of resemblances

between the properties of the material and those of Ni(NO)OH. Isomerization of this blue material to a green nonreducing substance containing divalent nickel is rapid (*2*, *15*). The ethanol product has also been formulated as $Ni(NO)(OC_2H_5)(OH)$ (*65*), and as either $Ni(NO)OH{\cdot}C_2H_5OH$ or $Ni(NO)(OC_2H_5){\cdot}H_2O$ (*2*). Its reducing properties also suggest the presence of monovalent nickel. This is further indicated by conversion of either Ni(NO)OH or its ethanol derivative into $K_2[Ni(CN)_3(NO)]$ by potassium cyanide (*2*), a product identical with that produced by reaction of nitric oxide with the nickel complex $K_2[Ni(CN)_3]$.

2. Metal nitrosyl halides: Numerous iron, cobalt, and nickel nitrosyl halides have been obtained by reacting nitric oxide with halogen derivatives of these metals. Representative are $Fe_2(NO)_4I_3$, prepared from $Fe(CO)_4I_2$ (*25*); $Fe(NO)_2I$, from iron nitrosyl carbonyl dissolved in benzene (*24*); Fe(NO)I, from decomposition of a pyridine addition compound prepared from $Fe(NO)_2I$ (*27*); $Fe(NO)_3Cl$, from anhydrous ferrous chloride in the presence of zinc (*27*); $Co(NO)_2I$, $Co(NO)_2Br$, and $Co(NO)_2Cl$, from anhydrous cobalt halides or from alcoholic solutions of the anhydrous halides in the cases of the iodide and bromide (*26*); and Ni(NO)I, Ni(NO)Br, and Ni(NO)Cl, from anhydrous nickel halides in the presence of halogen absorbers such as zinc or nickel (*27*). Ease of direct formation of these compounds from the anhydrous halides appears to decrease in the orders Fe-Co-Ni and I-Br-Cl.

Compounds of this type are characterized by their thermal instabilities at elevated temperatures, although some of the materials can be sublimed without decomposition at lower temperatures. Most of the substances appear to be coordinately unsaturated and react readily with such donors as pyridine and orthophenanthroline (*27*). Even more striking are the reducing properties which indicate monovalence among the metals. Thus, nickel nitrosyl iodide yields red $K_2[Ni(CN)_3(NO)]$ with potassium cyanide, blue $K_3[Ni(S_2O_3)_2(NO)]$ with potassium thiosulfate, and free silver and silver iodide with ammoniacal silver nitrate (*27*). The peculiar compound $Fe_2(NO)_4I_3$ is believed to contain both monovalent and divalent iron (*25*).

In an attempt to systematize materials of this sort, Seel (*76*) suggested a nitrosyl displacement series, comparable with Grimm's hydride displacement series, by which the addition of *n* molecules of nitric oxide converts a metal atom into pseudo-atom *n* groups to the right in the periodic classification. Thus, in this region the true and pseudo atoms would be:

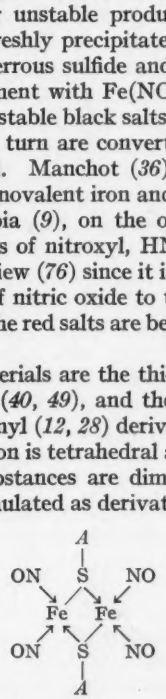
Fe	Co	Ni	Cu
	Fe(NO)	Co(NO)	Ni(NO)
		$Fe(NO)_2$	$Co(NO)_2$
			$Fe(NO)_3$

Compounds of the type Co(NO)X are known only as addition products, such as $Co(NO)I{\cdot}6C_5H_5N$ (*26*). Among the pseudo-copper materials, Seel (*76*) has indicated probable monomerism for materials containing the $Fe(NO)_3$ group, dimerism for materials containing the $Co(NO)_2$ group, and tetramerism for materials containing the Ni(NO) group as being necessary for four-coordination. In support he has listed comparable cuprous complexes of the types $[CuB_3I]$, $[CuB_2I]_2$, and $[CuBI]_4$, where the coordinated *B* groups are neutral molecules.

3. Metal nitrosyl thio compounds: The literature records a bewildering array of nitrosyl derivatives containing sulfur. The true structures of most of these compounds await elucidation, and much of the controversy concerning them is based upon conflicting lines of chemical evidence. While these materials appear to contain formally monovalent metals, the exact oxidation states of the metals are not known with certainty. The discussion which follows will consider some representatives of this class.

Iron forms a number of series of derivatives of the general formula $Fe(NO)_2SA$, where *A* may be hydrogen or a metal, a sulfonic group, or an alkyl or aryl group (*15*). Perhaps the best known of these compounds are Roussin's red salts, $M[Fe(NO)_2S]$, where M is a monovalent cation (*e. g.*, Na^+, K^+, NH_4^+). These salts are obtained as rather unstable products in reactions of nitric oxide with freshly precipitated ferrous sulfide or with mixtures of ferrous sulfide and alkali polysulfides (*15*). Upon treatment with $Fe(NO)SO_4$ they are converted to the more stable black salts of Roussin, $M[Fe_4(NO)_7S_3]$, which in turn are converted back to the red salts by free alkali. Manchot (*36*) believes these red salts to contain monovalent iron and coordinated nitrosyl groups. Cambia (*9*), on the other hand, regards them as derivatives of nitroxyl, HNO. The former is the more favored view (*76*) since it is in accord with the general tendency of nitric oxide to transfer an electron and coordinate. The red salts are believed to be dimeric (*76*).

Comparable materials are the thiosulfato derivative, $M^I[Fe(NO)_2SSO_3]$ (*40*, *49*), and the ethyl (*28*, *40*, *41*, *42*, *49*, *67*) and phenyl (*12*, *28*) derivatives, $Fe(NO)_2SR$. On the view that iron is tetrahedral and four-coordinate and that these substances are dimeric, all such compounds can be formulated as derivatives of



where the sulfurs act as bridging groups.

Corresponding cobalt and nickel compounds are less well characterized. Salts yielding the ions $[Co(NO)_2(S_2O_3)]^=$ and $[Ni(NO)(S_2O_3)_2]^=$ have been obtained in the presence of alkali thiosulfate and nitric oxide (*36*). Ethyl mercaptan derivatives, $Co(NO)_2SC_2H_5$ (*47*) and $Ni(NO)SC_2H_5$ (*46*), have been prepared by a reaction

$$M(SR)_2 + n\ NO \rightarrow M(NO)_{n-1}\ SR + NOSR$$

which appears to be general for iron, cobalt, and nickel (*41*), *n* being 3 for iron and cobalt and 2 for nickel.

Such compounds are probably examples of the general series, $Co(NO)_2SA$ and $Ni(NO)SA$. Evidence for the monovalence of cobalt and nickel seems more conclusive (*37*) than evidence that they are associated with hyponitrite radicals (*67, 68*). The molecular complexities of such materials have not been established, and they should perhaps be written $[Co(NO)_2SR]_x$ and $[Ni(NO)SR]_x$.

C. Nitrosyl Compounds of the Type $M^{II}(NO)_xA_y$: Interpretation of compounds classifiable under this heading in terms of exact oxidation states of the metals is again questionable. Actual assignment of divalence is more formal in most instances than justifiable on the basis of experimental evidence.

Absorption of nitric oxide by ferrous salt solutions up to a limiting ratio of $1NO:1Fe^{++}$ is well known (*30, 31, 35, 53*) and is the basis for the familiar brown-ring test for nitrites and nitrates. The reaction is readily reversed (*31, 44*), especially by increased temperature, and loss of nitric oxide regenerates ferrous salts unchanged. Solid ferrous salts do not, in general, absorb nitric oxide, and the instabilities of the products in solution render their recovery in the solid state exceedingly difficult. At low temperatures a crystalline acid phosphate, $Fe(NO)HPO_4$, has been precipitated from a solution of the sulfate derivative (*35*), and a brownish crystalline selenate, $Fe(NO)SeO_4{\cdot}4H_2O$, has been precipitated from aqueous ferrous selenate solution saturated with nitric oxide by absolute alcohol also saturated with nitric oxide (*47*). Stable dithiocarbamate derivatives, $Fe(NO)(R_2NCS_2)_2$, containing a variety of substituted groups have been reported (*10*), as has also a stable ethyl xanthate derivative containing two nitrosyl groups, $Fe(NO)_2(SCSOC_2H_5)_2$ (*13, 38*).

Although such ferrous nitrosyl complexes are commonly encountered as brown solutions, green and red materials are also known (*45*). Transference studies (*31*) indicate that combination may involve either cationic or anionic iron, anionic addition occurring in the presence of many acids, methanol, ethanol, acetone, or acetoacetic ester, and cationic addition in neutral solutions or in the presence of pyridine. Color migration in applied fields indicates the brown materials to be cationic, the green anionic, and the red neutral. The existence of more than a single type of complex is further substantiated by absorption spectra studies (*48, 75*), but exact information relative to types of bonding and true compositions of the materials awaits further investigations. A somewhat analogous ferric derivative, $Fe_2(NO)_2(SO_4)_3$, has also been reported (*33*).

In the presence of the free acids cupric sulfate, chloride, and bromide solutions absorb nitric oxide up to a limiting ratio of $1NO:1Cu^{++}$ (*31, 34, 35*). The resulting deep blue-violet solutions appear to contain but a single complex (*48, 75*), and this is believed to be anionic in character because of the presence of copper-containing anions in the absorbing solutions. A suggestion that they are molecular complexes has also been advanced (*35*) but not strongly supported.

The formation of the palladous nitrosyl derivatives, $Pd(NO)_2Cl_2$ and $Pd(NO)_2SO_4$, by direct absorption of nitric oxide (*52*) appears to be comparable. It seems also that the interesting nitrosyl dithiocarbamate derivatives of chromium, $Cr(NO)_2(R_2NCS_2)_2$, prepared by Malatesta (*32*), are representative of this class. These materials are obtained by treating chromous acetate with alcoholic R_2NCS_2Na (R = ethyl or propyl) and dry nitric oxide at 0°C. in an atmosphere of carbon dioxide. The ethyl derivative is described as a stable red solid and the propyl derivative as a red oil. Both materials are nonionic, but the oxidation state of chromium, while formally +2, is not known with certainty (*32*).

Much additional information is necessary for a complete understanding of this class of compounds, especially information concerning the oxidation states of the metals and the nature of the nitrosyl groups.

D. Nitrosyl Derivatives Containing Groups of the Type $[MA_5(NO)]^{+n}$: Representative of this class are compounds yielding the anions $[Mn(CN)_5(NO)]^{=}$ (*6, 51*), $[Fe(CN)_5(NO)]^{=}$ (*4, 15, 59, 77*), $[Ru(CN)_5(NO)]^{=}$ (*39*), $[Co(NO_2)_5(NO)]^{=}$ (*17*), $[RuCl_5(NO)]^{=}$ (*29*), and $[OsCl_5(NO)]^{=}$ (*83*). These ions satisfy the demands imposed by the transfer of one electron and the subsequent coordination of an electron pair by the resulting positive nitrosyl group.

Best characterized is the series $[M(CN)_5(NO)]^{-n}$, of which the iron compounds, or nitroprussides, are the best-known examples. Nitroprussides are obtained by a variety of reactions, perhaps the commonest of which is treatment of alkali ferrocyanides with nitric acid. By an analogous reaction involving a ruthenocyanide the potassium compound, $K_2[Ru(CN)_5(NO)]{\cdot}2H_2O$, has been prepared (*39*), but the manganese derivatives are prepared by saturating manganous acetate solution with nitric oxide in the presence of alkali cyanide (*6, 51*). The nitroprussides develop intense violet colorations with alkali sulfides (Gmelin reaction) but not with hydrogen sulfide (*71, 73*), due perhaps to the formation of $[Fe(CN)_5(NOS)]^{=}$ (*59*), and intense red colorations with alkali sulfites (Bödecker reaction) (*74*), due perhaps to the formation of $[Fe(CN)_5(NOSO_3)]^{=}$ (*59, 74*). Comparable color reactions have been noted for certain organic sulfur compounds. The insolubility of the mercuric nitroprusside has been suggested as a basis for quantitative determination of the radical (*78*). Recent work (*72*) has confirmed the ferrous condition of iron in the nitroprussides and has indicated that one CN group is attached to iron through nitrogen and the other four through carbon, giving *cis-trans* isomerism.

The pink and black compounds containing the group $[Co(NH_3)_5(NO)]^{++}$ are of particular theoretical interest. Both types of materials result from the absorption of nitric oxide by cobaltous salt solutions containing ammonia (*70, 82*). The black compounds are unstable with respect to the pink and evolve nitric oxide upon treatment with acids, whereas the pink compounds do not. The only black compounds which have been reported are the chloride and the iodate, but many examples of the pink series are known. Members of the

black series are paramagnetic, while those of the pink series are diamagnetic (*17, 23, 55, 56, 61, 63*). The pink isomers are generally believed to contain trivalent cobalt and the negative nitrosyl group (*55, 77*) as has been pointed out in the discussion of structural possibilities. The constitution of the black isomers is not so well understood. The suggested resonance between mono- and trivalent cobalt (*56*) appears untenable because it involves different numbers of unpaired electrons (*55*). The assumption that the black complexes contain divalent cobalt (*23, 55*) seems more probable. While it is generally agreed that the cobalt is coordinately linked to six nitrogen atoms, presumably through d^2sp^3 bonds, a number of suggestions as to exact constitution have been offered. Among these are the presence of two three-electron bonds in the nitrosyl group (*61*), equilibrium between normal and excited states due to the odd electron in nitric oxide (*23*), and a dimeric structure, $[Co(NH_3)_5(NO)]_2^{+4}$, containing two unpaired electrons (*55*). These possibilities are in agreement with the paramagnetic properties of the black materials, but it is still questionable whether these black derivatives can be strictly compared with other nitrosyl complexes.

A few other materials of this general type have been reported. Thus, nickel carbonyl is said to yield both $[Ni(NH_3)_5(NO)]NO_2$ and $[Ni(NH_3)_5(NO)]NO_3$ upon treatment with nitric oxide and ammonia (*16*). The ruthenium compounds $[Ru(NH_3)_4Cl(NO)]Br_2$ and $[Ru(NH_3)_4(H_2O)(NO)]Cl_3$ have also been prepared (*69*). These compounds are both diamagnetic (*69*) and may contain tetravalent ruthenium and negative nitrosyl groups (*55*).

E. Miscellaneous Nitrosyl Compounds: Among such miscellaneous derivatives are the nitrosyl dithiocarbamates of ruthenium. These are red, crystalline, diamagnetic substances of the type $Ru(NO)(R_2NCS_2)_3$, where R may be methyl or ethyl (*11*), and are obtainable either from ruthenium(III) dithiocarbamates and nitric oxide or alkali dithiocarbamates and the ruthenium complex $K_2[RuCl_5(NO)]$.

Treatment of saturated ammonium or potassium chloroplatinite solution with nitric oxide for three to four days is reported to yield a green solution from which tetrammine platinum(II) chloride solution precipitates reddish gray $[Pt(NH_3)_4][Pt(NO)Cl_3]$ and pyridine precipitates $[Pt(NO)(pyr)Cl_2]$ (*22*). Striking resemblances between these compounds and the corresponding ethylene and carbonyl derivatives exist (*22*), and the *trans* configuration of the pyridine-containing derivative suggests that the nitrosyl group is *trans*-directing (*22*).

Of considerable interest are the so-called black salts of Roussin (*15, 77*), which have already been mentioned. These materials are of the type $M^I[Fe_4(NO)_7S_3]$, where M^I may be Na^+, K^+, Rb^+, Cs^+, NH_4^+, or Tl^+ (*28, 54*). They can be prepared by the reaction of nitrite and sulfide ions with ferrous salt solutions, by the reaction of suspensions of freshly precipitated ferrous sulfide or of mixtures of ferrous chloride and alkali polysulfides with nitric oxide, or from the red salts as already outlined. The exact structure of the $[Fe_4(NO)_7S_3]^-$ has not been determined. It is believed that each iron is four-coordinate, with sulfurs acting as bridging groups to link the four iron tetrahedra together and nitrosyl groupings occupying the remaining positions (*76*).

Absorption of nitric oxide by alkaline sulfite solutions yields compounds of the type $M_2^ISO_3 \cdot 2NO$ (*80*). Hyposulfites yield the same products with nitric oxide (*18*). Reduction to amido and hydrazino sulfurous acids indicates the presence of the N—S linkage in such materials, and conversion of freshly precipitated ferrous sulfide to Roussin's black salts by these substances suggests the presence of individual NO groups (*80*). It has been suggested that both nitrosyl groups are coordinated to the sulfur, giving $[O_3S(NO)_2]^-$ ions (*80*). On this assumption certain analogies between these materials and thiosulfates are easily explained (*19, 80*).

Fremy's salt, $(KSO_3)_2NO$ (*18, 20*), also deserves mention, especially since it is an odd molecule. As obtained by oxidation of potassium hydroxylamine disulfonate, it forms yellow crystals which dissolve to a blue solution in water. The solid is diamagnetic and the solution paramagnetic (*3*), suggesting a pairing of electron spins by dimerization in the solid state followed by unpairing and monomer formation in solution. The structure of this compound is not known nor has the role of the nitrosyl grouping been elucidated. The material is also of some interest in that it in turn absorbs nitric oxide, forming $(KSO_3)_2NO \cdot NO$ (*20*).

CONCLUSION

The variety of compounds containing apparently coordinated nitrosyl groups and the paucity of structural data concerning these materials are indicative of the importance of further fundamental and comprehensive investigations in this field. It is to be hoped that such work will permit classification of these compounds upon a sounder basis than the formalized one used in this discussion. The nitrosyl grouping is truly an unusual grouping among chemical materials

LITERATURE CITED

(1) ANDERSON, J. S., WITH W. HIEBER, *Z. anorg. allgem. Chem.*, **208**, 238 (1932).
(2) ANDERSON, J. S., *ibid.*, **229**, 357 (1936).
(3) ASMUSSEN, R. W., *ibid.*, **212**, 317 (1933).
(4) BLANCHARD, A. A., *Chem. Revs.*, **26**, 409 (1940).
(5) BLANCHARD, A. A., AND P. GILMONT, *J. Am. Chem. Soc.*, **62**, 1192 (1940).
(6) BLANCHARD, A. A., AND F. S. MAGNUSSON, *ibid.*, **63**, 2236 (1941).
(7) BLANCHARD, A. A., J. R. RAFTER, AND W. B. ADAMS, JR., *ibid.*, **56**, 16 (1934).
(8) BROCKWAY, L. O., AND J. S. ANDERSON, *Trans. Faraday Soc.*, **33**, 1233 (1937).
(9) CAMBIA, L., *Z. anorg. allgem. Chem.*, **247**, 22 (1941).
(10) CAMBIA, L., AND A. CAGNASSO, *Atti accad. Lincei*, **13**, 254, 809 (1931).
(11) CAMBIA, L., AND L. MALATESTA, *Rend. ist. lombardo sci.*, **71**, 118 (1938).
(12) CAMBIA, L., AND L. SZEGÖ, *Atti accad. Lincei*, **4**, 491 (1926).
(13) CAMBIA, L., AND L. SZEGÖ, *ibid.*, **13**, 93 (1931).
(14) COLEMAN, G. W., AND A. A. BLANCHARD, *J. Am. Chem. Soc.*, **58**, 2160 (1936).

(15) EMELÉUS, H. J., AND J. S. ANDERSON, "Modern Aspects of Inorganic Chemistry," D. Van Nostrand Company, Inc., New York, **1938**, pp. 407–11, 413–9, 430–1.
(16) FRAZER, J. C. W., AND W. E. TROUT, Jr., *J. Am. Chem. Soc.*, **58**, 2201 (1936).
(17) FRAZER, J. H., AND N. O. LONG, *J. Chem. Phys.*, **6**, 462 (1938).
(18) GEHLEN, H., *Ber.*, **64B**, 1267 (1931).
(19) GEHLEN, H., *ibid.*, **65B**, 1130 (1932).
(20) GEHLEN, H., *ibid.*, **66B**, 292 (1933).
(21) GELMAN, A., *Compt. rend. acad. sci. U.R.S.S.*, **24**, 549 (1939).
(22) GELMAN, A., AND Z. P. MAXIMOVA, *ibid.*, **24**, 748 (1939).
(23) GHOSH, S. P., AND P. RÂY, *J. Indian Chem. Soc.*, **20**, 409 (1943).
(24) HIEBER, W., AND J. S. ANDERSON, *Z. anorg. allgem. Chem.*, **211**, 132 (1933).
(25) HIEBER, W., AND G. BADER, *ibid.*, **190**, 193 (1930).
(26) HIEBER, W., AND R. MARIN, *ibid.*, **240**, 241 (1939).
(27) HIEBER, W., AND R. NAST, *ibid.*, **244**, 23 (1940).
(28) HOFMANN, K. A., AND O. F. WEIDE, *Z. anorg. Chem.*, **9**, 295 (1895).
(29) JOLY, A., *Compt. rend.*, **107**, 994 (1888).
(30) KOHLSCHÜTTER, V., AND M. KUTSCHEROFF, *Ber.*, **40**, 873 (1907).
(31) KOHLSCHÜTTER, V., AND P. SAZANOFF, *ibid.*, **44**, 1423 (1911).
(32) MALATESTA, L., *Gazz. chim. ital.*, **70**, 729, 734 (1940).
(33) MANCHOT, W., *Ann.*, **372**, 179 (1910).
(34) MANCHOT, W., *ibid.*, **375**, 308 (1910).
(35) MANCHOT, W., *Ber.*, **47**, 1601 (1914).
(36) MANCHOT, W., *ibid.*, **59B**, 2445 (1926).
(37) MANCHOT, W., *Ann.*, **459**, 47 (1927).
(38) MANCHOT, W., AND S. DAVIDSON, *Ber.*, **62B**, 681 (1929).
(39) MANCHOT, W., AND J. DÜSING, *ibid.*, **63B**, 1226 (1930).
(40) MANCHOT, W., AND E. ENK, *Ann.*, **470**, 275 (1929).
(41) MANCHOT, W., AND H. GALL, *Ber.*, **60B**, 2318 (1927).
(42) MANCHOT, W., AND H. GALL, *ibid.*, **61B**, 2393 (1928).
(43) MANCHOT, W., AND H. GALL, *Ann.*, **470**, 271 (1929).
(44) MANCHOT, W., AND H. HAUNSCHILD, *Z. anorg. allgem. Chem.*, **140**, 22 (1924).
(45) MANCHOT, W., AND F. HUTTNER, *Ann.*, **372**, 153 (1910).
(46) MANCHOT, W., AND Fr. KAESS, *Ber.*, **60B**, 2175 (1927).
(47) MANCHOT, W., AND E. LINCKH, *Z. anorg. allgem. Chem.*, **140**, 37 (1924).
(48) MANCHOT, W., AND E. LINCKH, *Ber.*, **59B**, 406 (1926).
(49) MANCHOT, W., AND E. LINCKH, *ibid.*, **59B**, 412 (1926).
(50) MANCHOT, W., AND W. J. MANCHOT, *Z. anorg. allgem. Chem.*, **226**, 385 (1936).
(51) MANCHOT, W., AND H. SCHMID, *Ber.*, **59B**, 2360 (1926).
(52) MANCHOT, W., AND A. WALDMÜLLER, *ibid.*, **59B**, 2363 (1926).
(53) MANCHOT, W., AND K. ZECHENTMAYER, *Ann.*, **350**, 368 (1906).
(54) MARCHLEWSKI, L., AND J. SACHS, *Z. anorg. Chem.*, **2**, 175 (1892).
(55) MELLOR, D. P., AND D. P. CRAIG, *J. Proc. Roy. Soc. N. S. Wales*, **78**, 25 (1944).
(56) MILWARD, J. L., W. WARDLAW, AND W. J. R. WAY, *J. Chem. Soc.*, 233 (1938).
(57) MOELLER, T., J. CHEM. EDUC., **23**, 441 (1946).
(58) MOND, R. L., AND A. E. WALLIS, *J. Chem. Soc.*, **121**, 32 (1922).
(59) MORGAN, G. T., AND F. H. BURSTALL, "Inorganic Chemistry: A Survey of Modern Developments," W. Heffer and Sons, Ltd., Cambridge, **1936**, pp. 364–71.
(60) ORMONT, B., *Acta Physicochim. U.R.S.S.*, **12**, 159 (1940).
(61) PAULING, L., *J. Am. Chem. Soc.*, **53**, 3225 (1931).
(62) PAULING, L., "The Nature of the Chemical Bond," 2nd Ed., Cornell University Press, Ithaca, **1940**, pp. 250–8, 269–70.
(63) RÂY, P., AND H. BHAR, *J. Indian Chem. Soc.*, **5**, 497 (1928).
(64) REIFF, F., *Z. anorg. allgem. Chem.*, **202**, 375 (1931).
(65) REIHLEN, H., *ibid.*, **230**, 223 (1937).
(66) REIHLEN, H., A. GRUHL, G. VON HESSLING, AND O. PFRENGLE, *Ann.*, **482**, 161 (1930).
(67) REIHLEN, H., AND A. VON FRIEDOLSHEIM, *ibid.*, **457**, 71 (1927).
(68) REIHLEN, H., A. VON FRIEDOLSHEIM, AND W. OSWALD, *ibid.*, **465**, 72 (1928).
(69) ROSENBOHM, E., *Z. phys. Chem.*, **93**, 693 (1919).
(70) SAND, J., AND O. GENSSLER, *Ber.*, **36**, 2083 (1903).
(71) SAS, F.-E. RAURICH, *Anales soc. españ. fís. quím.*, **34**, 419 (1936).
(72) SAS, F.-E. RAURICH, *Anales fís. quím. (Spain)*, **39**, 55 (1943).
(73) SCAGLIARINI, G., *Atti congr. naz. chim. pura applicata* 4th Cong., (1932), **1933**, p. 597.
(74) SCAGLIARINI, G., *Atti accad. Lincei*, **22**, 155 (1935).
(75) SCHLESINGER, H. I., AND A. SALATHE, *J. Am. Chem. Soc.*, **45**, 1863 (1923).
(76) SEEL, F., WITH W. HIEBER, *Z. anorg. allgem. Chem.*, **249**, 308 (1942).
(77) SIDGWICK, N. V., AND R. W. BAILEY, *Proc. Roy. Soc. London*, **A144**, 521 (1934).
(78) TOMÍČEK, O., AND J. KUBÍK, *Collection Czechoslov. Chem. Commun.*, **9**, 377 (1937).
(79) WARDLAW, W., *Ann. Reps.*, **31**, 99 (1934).
(80) WEITZ, E., AND F. ACHTERBERG, *Ber.*, **66B**, 1718, 1728 (1933).
(81) WELCH, A. J. E., *Ann. Reps.*, **38**, 71 (1941).
(82) WERNER, A., AND P. KARRER, *Helv. chim. acta.*, **1**, 54 (1918).
(83) WINTREBERT, M. L., *Ann. chim. phys.*, [7], **28**, 15 (1903).
(84) ZINTL, E., AND A. HARDER, *Ber.*, **66B**, 760 (1933).

METHIONINE

The shade of Paracelsus, the 16th century founder of chemotherapy, may well be proud of what he started. He was a great believer in the use of sulfur in medicine, and now in 1946 it is a sulfur compound, the amino acid methionine, which is receiving spotlight attention from research chemists and physicians alike.

It is one of the virtues of modern research that as soon as a chemical is shown by one group to be of important value, others discover ways of making it not only purer but vastly less expensive. Thus it is that Glenn Haskell, president of United States Industrial Chemicals, Inc., has recently announced a commercially practical method for making methionine without the necessity of extracting it from natural foodstuffs. The new price will be about one-fortieth of the former quotation of several hundred dollars a pound for a minute quantity.

Adequate supplies of methionine are expected to revolutionize the treatment and preoperative care of peptic ulcer and other surgical cases, to say nothing of liver damage, poisoning, burn, and shock victims.

The full descriptive name of methionine is gamma methyl-thiol alpha amino normal butyric acid, and indicates that the several features of the molecule may have correspondingly different roles of importance to play in the human body. This is correct, for not only does some of the methionine we eat in our protein foods serve as a building block *per se* of our own muscles and fibres, but the rest of it yields valuable fragments for the proper behavior of our nerves, for the breathing of our cells, for the trussing and strengthening of new tissue (the sulfur really acts as it does in vulcanizing rubber!), for decontaminating poisons of several types, and for furnishing energy. The amount of methionine in proteins is too small to furnish a convenient therapeutic dose without giving the needy person too large a bulk of protein, or a vile-tasting amino acid mixture made from split proteins.

With this amino acid increasingly available, convenient dosages of other proteins, such as casein and yeast, enriched with it, can be used to block out the vicious cycle of nervousness, poor digestion, and weakened tissues which is responsible for so much irritable misbehavior of men in all walks of life.—Reprinted from the *Research Viewpoint* (Number 47).

A Kjeldahl Determination of Protein for General Chemistry

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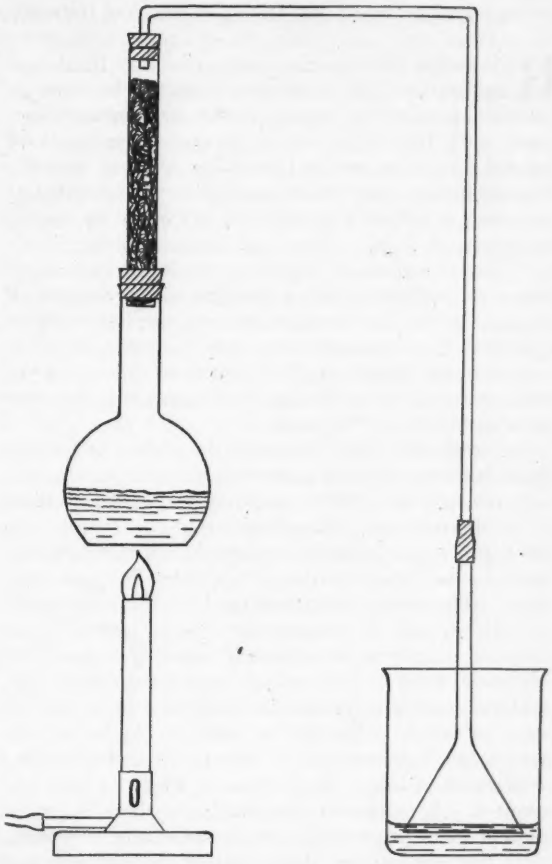
THE college freshman often developes a desire to graduate from "test tube" chemistry, asking for something of different character. Experiments of quantitative nature are finding popularity, especially for students who have already had a course in high-school chemistry. A Kjeldahl determination of nitrogen and protein in a food, besides being quantitative, has other attractive objects. It can be offered as an experiment during the study of nitrogen and its compounds where it emphasizes the role of nitrogen and protein in nutrition. Furthermore, it brings home some of the reactions and properties of ammonia. It should stimulate interest in volumetric quantitative analysis and also organic chemistry. An experiment in nutrition should appeal to the girls, whether they intend to become technicians or "make a home."

We have succeeded in modifying the usual Kjeldahl apparatus and procedure so that it may be safely and satisfactorily performed with the equipment usually available to beginners. Dog food in pellet form was chosen because of its convenient and dry form, an advantage quickly observed in weighing the sample and introducing it into the digestion flask.

Samples of approximately 0.75 g. are weighed to 0.5 mg. and introduced into a 250-ml. pyrex florence flask with approximately 10 g. of potassium sulfate, 1 g. of cupric sulfate, and 25 ml. of concentrated sulfuric acid. The flask and contents are heated in the hood, starting with a small flame which is gradually increased in size. Occasional swirling of the flask brings all matter in contact with the acid. Usually at the end of 30 minutes the mixture is clear green or blue with no carbonaceous matter, indicating that the digestion is complete.

While the digestion is in progress, the student may prepare the distillation delivery tube as shown in the diagram. This may be made from 6- to 8-mm. tubing. The exit end is attached to an inverted funnel to prevent "suck backs." It was found best to insert a section of 10 to 12-mm. tubing between the flask and delivery tube to serve as a Kjeldahl trap. We packed this with steel or glass wool as an added precaution to catch alkali spray, although with moderate distillation this packing was not necessary. The open end of the funnel dips into a beaker below the surface of 25 ml. of standardized 0.5 *N* HCl measured by a pipet.

When the digestion is complete, the flask and contents are allowed to cool partially and then 60 ml. of water are cautiously added. When all is in readiness, 50 ml. of 40 per cent NaOH is slowly poured down the neck of the flask to form a layer on the bottom. A piece or two of granulated zinc is added to prevent bumping during the distillation, and the delivery tube is immediately attached to the flask, the flask swirled



and clamped to a ring stand. It is best to clamp the delivery tube also to a stand. The contents of the flask are distilled for 25 minutes. Next, the funnel is removed from the beaker with rinsing, and the residual acid in the beaker titrated with standardized 0.5 *N* NaOH.

Calculations were made as below, but the authors give the method here merely as a suggestion.

Volume of original acid × normality — vol. of standard alkali × normality = milliequivalents of nitrogen

Meq. nitrogen × 14 = milligrams of nitrogen

$$\frac{\text{mg. nitrogen}}{\text{wt. sample in mgs.}} \times 100 = \%\ \text{nitrogen}$$

% nitrogen × 5.7 = % protein

The factor 5.7 was used since a large part of the protein of the dog food came from a cereal source.

BALANCING EQUATIONS

for

Organic Oxidation-Reduction Reactions

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REGARDLESS of the fact that a third-year college student in chemistry should be able to balance equations for organic oxidation-reduction reactions, very few textbooks or laboratory manuals of organic chemistry explain how to do this, and then the discussions are, more or less, limited to the oxidation or reduction of carbon when bonded to carbon, hydrogen, or oxygen (*5*, *7*, *8*). This topic concerning the oxidation and reduction of organic compounds, which includes the definition and determination of valences of elements in organic compounds and the balancing of equations for redox reactions, has been the subject of several recent papers (*1*, *2*, *3*) and from these, and the few treatments in textbooks, there appears to be quite an arbitrariness on the issue.

The student's chief interest is the ability to balance equations for oxidation-reduction reactions, and naturally teachers have chosen methods that seemed to them to be the quickest and easiest to apply—that is, the whole process of balancing equations, whether or not it involves the determination of valences, is quite arbitrary. The various methods used by different teachers fall into one of two systems—one in which, by individual techniques or empirical rules, the change in oxidation level is determined without knowing the oxidation states of the reactants and products, and the other in which the oxidation state of the initial and final stages is determined in order to obtain the valence or electron change. Regardless of which system was adopted, the methods described elsewhere have, in general, been extended to simple structures of carbon, hydrogen, and oxygen, thus omitting the oxidation and reduction of complex structures, or of nitrogen, sulfur, and the halogens. In addition to the element carbon, most organic compounds contain one or more of the eight elements hydrogen, oxygen, nitrogen, sulfur, and the halogens, and those which contain nitrogen, sulfur, and the halogens are too numerous and familiar to be omitted from any general treatment. The graduate student should be able to balance equations for the oxidation or reduction of such compounds. In this paper there is outlined a method that can be applied to balance equations for the oxidation or reduction of complex organic structures or of any of the nine elements commonly found in organic compounds—carbon, hydrogen, oxygen, nitrogen, sulfur, and the halogens.

The basic concepts and principles stated in the foregoing presentation are not original to the author (*14*) but merely formulated, organized, and their application demonstrated. Perhaps the method will be found to be a little tedious for simple cases of oxidation and reduction, but it is quite useful when considering the oxidation or reduction of complex structures or different oxidation levels of an element when in related classes of compounds.

Oxidation and reduction are defined as the loss or gain of electrons, respectively, and in inorganic reactions usually there is an actual transfer of electrons, but in organic reactions this exchange of electrons is not as clear-cut. In a compound constructed of covalent bonds, oxidation or reduction of an element perhaps is a matter of the relative nearness of the shared pairs of electrons of the bonds which that element makes (*9*). For example, due to the difference in electronegativity of the atoms in a carbon-hydrogen bond the pair of electrons are drawn in closer to the carbon atom, producing a formal negative charge on the carbon atom and a formal positive charge on the hydrogen atom, while in a carbon-chlorine bond the pair of electrons are drawn closer to the chlorine atom, producing a formal negative charge on the chlorine atom and leaving a formal positive charge on the carbon atom. Thus, in chlorination

$$\text{>C:H} \xrightarrow{Cl_2} \text{>C:Cl}$$

where a hydrogen atom is replaced by a chlorine atom, a shared pair of electrons is drawn away from the carbon atom and this removal, or shift, of electrons constitutes an oxidation (*4*, *5*, *10*, *11*, *12*).

In carbon-oxygen, carbon-nitrogen, carbon-sulfur, and carbon-halogen bonds, the pair of electrons are drawn away from the carbon, leaving the carbon atom with a formal positive charge and the other atoms with a formal negative charge. The same rule applies for multiple bonds, each bond contributing one positive charge to the carbon and a negative charge to the other atom. Thus, in a nitrile group, C≡N, the carbon atom has three positive formal charges and the nitrogen three negative formal charges.

This means that each C—H bond contributes one negative charge and each C—N, C—O, C—S, and C—halogen bond contributes one positive charge to the total formal charge on the carbon atom. This total formal charge, or "relative valence," we shall call the polar number and is obtained by taking the algebraic sum of these formal charges collecting on the carbon atom from its bonds. The electrons between two like atoms are attracted equally as much by both atoms so that there will not be a resulting formal charge on either atom from such bonds. The term, polar number, for

elements in organic compounds will be used similarly as the terms "oxidation state" or "valence" for elements in inorganic compounds (*13*, *14*).

The usual attachments made by the nine elements commonly found in organic compounds and the formal charges on each atom resulting from such bonds are indicated in Table 1. Pauling (*6*) gives the relative

TABLE 1

$\overset{-}{C}—\overset{+}{H}$	$\overset{-}{N}—\overset{+}{H}$	$\overset{-}{S}—\overset{+}{H}$
$C—C$	$\overset{-}{N}—\overset{+}{C}$	$\overset{-}{S}—\overset{+}{C}$
$C—\overset{+}{O}$	$N—N$	$S—S$
$C—\overset{+}{N}$	$\overset{-}{N}—\overset{+}{Cl}$	$S—\overset{+}{O}$
$C—\overset{+}{S}$	$\overset{-}{N}—\overset{+}{Br}$	$S—\overset{+}{N}$
$C—\overset{+}{X}$	$N—\overset{+}{O}$	$S—\overset{+}{Cl}$

electronegatives of these nine elements as follows: H, 2.1; C, 2.5; N, 3.0; O, 3.5; S, 2.5; F, 4.0; Cl, 3.0; Br, 2.8; I, 2.5.

The charges on the atoms in N—Cl, C—S, and C—I bonds are not predictable from Pauling's values of electronegativities, but the charges as indicated in Table 1 are the charges exhibited in such bonds.

To determine the polar number of any atom of these elements when in an organic compound, we add algebraically the formal charges from all of the bonds which that atom makes, including polar charges from coordinate covalent bonds. Several examples follow.

In methane, the carbon atom forms four C—H bonds (−4) so its polar number is −4. In ethane, each carbon atom forms three C—H bonds (−3) and one C—C bond (0) making its polar number −3. In nitromethane, the carbon atom forms three C—H bonds (−3) and one C—N bond (+1), making its polar number −2. The nitrogen atom forms one C—N bond (−1), three N—O bonds (+3) and has one positive polar charge (the structure of the nitro group is assumed to be $\overset{+}{N}\begin{matrix}\diagup \overset{-}{O} \\ \diagdown O\end{matrix}$) which gives a resulting +3 polar number for the nitrogen atom. In acetyl chloride, the carbonyl carbon atom forms two C—O bonds (+2), one C—Cl bond (+1), and one C—C bond (0), making its polar number +3. The chlorine atom forms one C—Cl bond so its polar number is −1.

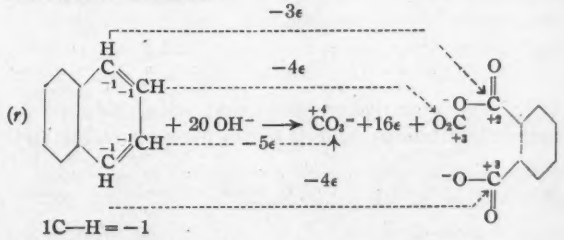
We see, then, that we can determine the oxidation state, or at least "relative valences," of the elements carbon, hydrogen, oxygen, nitrogen, sulfur, and the halogens when in organic compounds. This system, however, requires a knowledge of two things. First, one must know the structure of the compound, and second, one must know the relative electronegativities of the above nine elements. These are not drawbacks because the student is expected to know the structure of the compound with which he is working and he knows the relative position of these elements in the periodic table at the time he is taught how to balance oxidation and reduction equations. It is easy to decide that carbon is positive with respect to all the elements considered except hydrogen and that nitrogen and sulfur are both positive with respect to oxygen. A question may arise in regard to N—Cl, C—S, and C—I bonds, but these may quickly be learned.

This approach in determining the oxidation state of elements in organic compounds may have some significance. For instance, we have stated that bonds between like atoms do not affect the polar number or oxidation state of the atoms, and it is observed that elements in their elemental state, with particular reference to diatomic elements, are considered to be in oxidation states of zero. In hydrazine, $H_2N—NH_2$, each nitrogen atom makes two N—H bonds (−2) and one N—N bond (0), and its oxidation state, or valence, is considered by inorganic chemists to be −2.

In this presentation there are several second-order effects that have been neglected, such as, assuming (*a*) the formal charge from a multiple bond between two atoms to be the same multiple of the charge from a single bond between those two atoms (*i. e.*, in $R_2C{=}O$, C = +2 and O = −2), (*b*) the formal charge on a carbon atom is the same when bonded to oxygen, nitrogen, sulfur, or the halogens although these elements have different electronegativities, and (*c*) inductive and resonant effects from neighboring groups do not affect the polar number of an atom. These factors are interesting and significant but do not alter the number of equivalents involved when calculating the changes in polar numbers.

The two most widely used methods in balancing equations for inorganic reactions are the valence change and the ion-electron or half-reaction methods. The average student learns and uses one of these methods without any particular difficulty. Let us consider several oxidation-reduction reactions, apply the proposed method to determine the polar numbers of the elements undergoing oxidation or reduction, and use either the ion-electron or valence change method to balance the equations. Beneath the organic substances are listed the type of bonds formed by the atom being oxidized or reduced and its formal charges totalled to give its polar number.

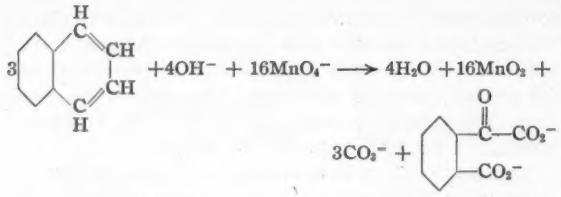
1. The oxidation of naphthalene with alkaline permanganate to produce phthalaldehydic acid by the ion-electron method:



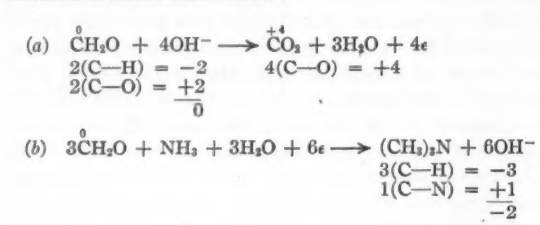
(*r*)

(*s*) $2H_2O + MnO_4^- + 3\epsilon \longrightarrow MnO_2 + 4OH^-$

Three times equation (*r*) plus 16 times equation (*s*), followed by cancellation, gives



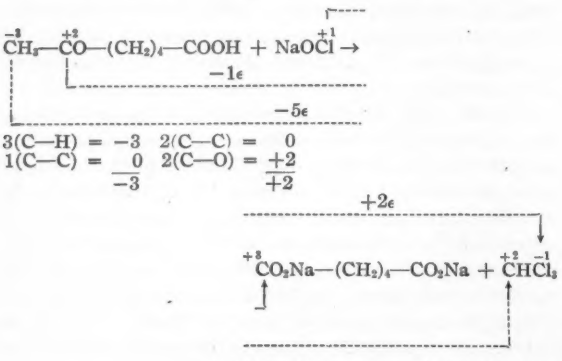
2. Formaldehyde reacts with ammonia to give carbon dioxide plus trimethylamine. The ion-electron method is illustrated below:



Three times equation (*a*) plus twice equation (*b*), followed by cancellation, gives

$$9CH_2O + 2NH_3 \rightarrow 2(CH_3)_3N + 3CO_2 + H_2O$$

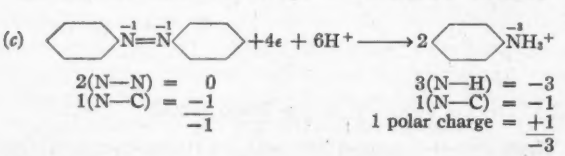
3. The oxidation of 6-keto-heptanoic acid with sodium hypochlorite to produce sodium adipate plus chloroform by the valence change method:



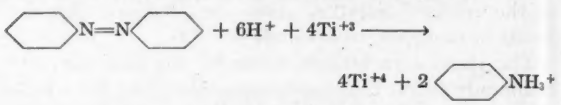
To remove the six electrons from the two carbon atoms, it requires three mols of sodium hypochlorite. Then, after balancing the oxygen and hydrogen atoms we get the final balanced equation:

$$CH_3—CO—(CH_2)_4—COOH + 3NaOCl \longrightarrow CO_2Na—(CH_2)_4—CO_2Na + 3CHCl_3 + H_2O + NaOH$$

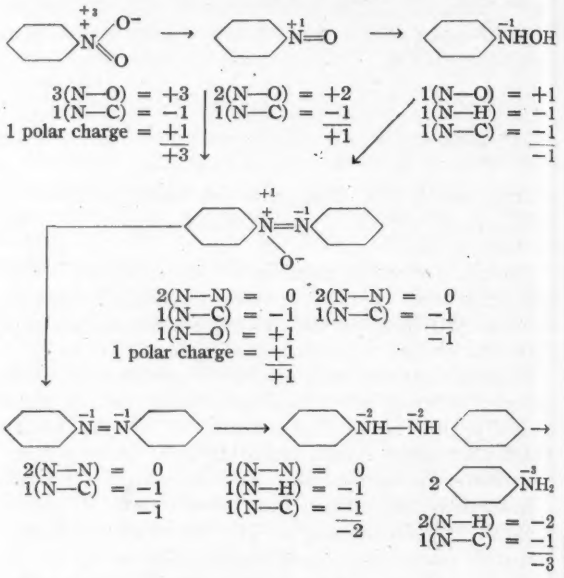
4. The quantitative reduction of azobenzene to aniline by titanous chloride by the ion-electron method:



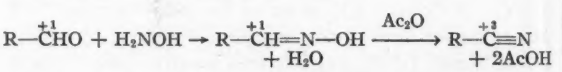
Equation (*c*) plus four times equation (*d*) gives



The proposed system to determine the oxidation states of the elements in organic compounds is convenient when we consider nitrogen in the various stages of the alkaline reduction of nitrobenzene. The polar number of the nitrogen atoms are indicated below.



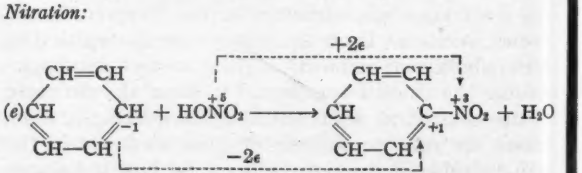
Consider the series of reactions,



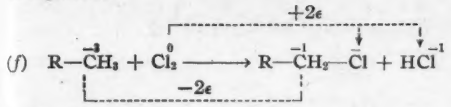
Both stages consist of a removal of water; still, the carbonyl carbon atom changes from a valence of +1 to +3. Frequently it is asked, in which step does the oxidation occur? If we determine the polar numbers, however, we see that in the aldehyde and oxime the carbon atoms are of equal oxidation states—that is, +1—while in the nitrile it has changed to +3, so that the oxidation takes place in the second step. Here, the nitrogen atom is reduced from −1 to −3 while the carbon atom is oxidized from +1 to +3.

Other authors have pointed out and shown that some classical organic reactions are oxidation-reduction reactions. This is borne out when we consider the change in polar numbers as illustrated below:

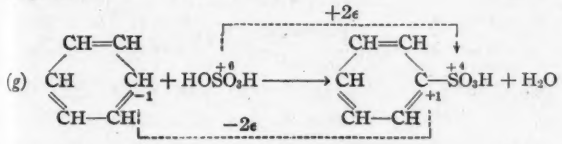
Nitration:



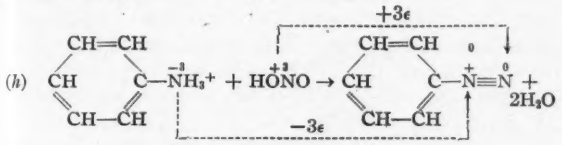
Halogenation:



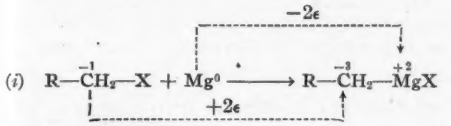
Sulfonation:



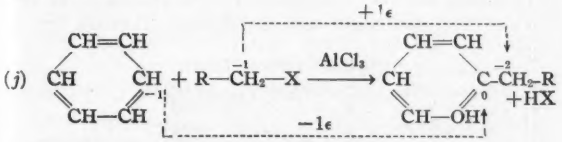
Diazotization:



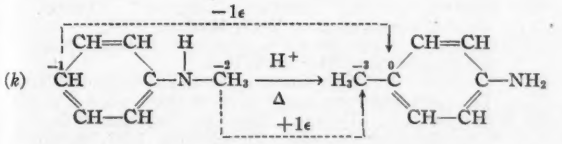
Grignard Formation:



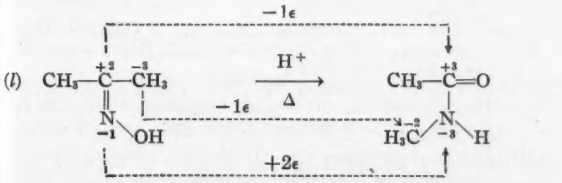
Friedel-Crafts reaction:



Rearrangements—
Hofmann:

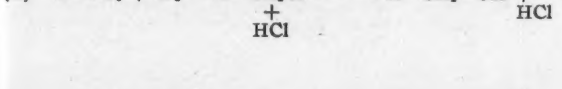


Beckmann:

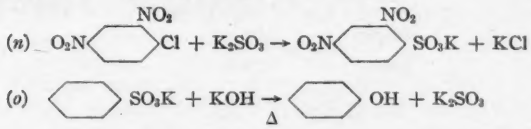


Many other examples could be listed. Reactions such as hydrolyses, ammonolyses, or esterification, on the other hand, are not oxidation-reduction reactions because they bring about no changes in oxidation state.

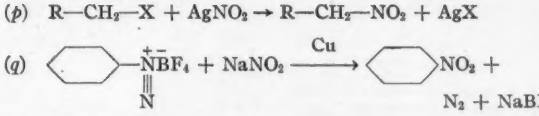
It will become apparent that changes in polar numbers through such reactions as chlorination, sulfonation, and nitration actually constitute changes in oxidation states when we consider the following reactions:



Without doubt, in reaction (*m*) the Cl_2 has been reduced; therefore, something has been oxidized. It seems reasonable to say that the carbon was oxidized and that its oxidation took place in the chlorination rather than the hydrolysis.



Reactions (*n*) and (*o*) show that the sulfur in benzene sulfonic acid is of the same oxidation state as in potassium sulfite which indicates that the sulfur in sulfuric acid was reduced in reaction (*g*) above and, therefore, the sulfonated carbon atom was oxidized.



Reactions (*p*) and (*q*) show that the nitrogen atom in nitro compounds is of the same oxidation state as in nitrites; hence, in nitrations with nitric acid the nitrogen atom is reduced and the nitrated carbon atom is oxidized.

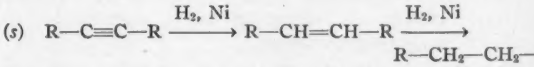
It is interesting to note that the order of increasing tendency to react corresponds somewhat to the order of oxidation potentials of nitric acid, sulfuric acid, and the halogens.

	F_2	$>Cl_2$	$>Br_2$	$>HNO_3$	$>H_2SO_4$	$>I_2$
E_0 =	−2.85	−1.36	−1.07	−0.94	−0.2	−0.54

(E greater in high $[H^+]$)

Probably most organic oxidation-reduction reactions involve the oxidation or reduction of carbon and, for this reason, it is convenient to have a table which indicates the polar number of carbon in different classes of compounds. In Table 2, various classes of organic compounds and certain members are listed according to the polar number of the carbon atom (the starred carbon atom when others are present of different polar number).

From the table we see that primary, secondary, and tertiary carbon atoms are of different oxidation states. It will be observed that carbon atoms in alkanes, alkenes, and alkynes are of different oxidation states when we consider reaction (*s*), in which hydrogen is



oxidized in each step. Hence carbon must be successively reduced. In reaction (*t*), where sulfur is reduced, carbon must be oxidized.

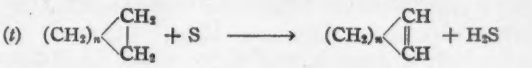
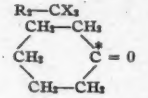
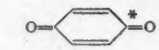
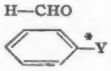
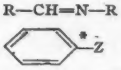
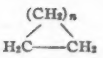
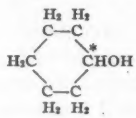


TABLE 2

−4	−3	−2	−1	0	+1	+2	+3	+4
CH_4	$R—CH_3$	$R_2—CH_2$	R_3CH	$R_4—C$	R_3COH	$R_2—CO$	$R—COOH$	CO_2
	$R—CH_2Na$	$R—CH=\overset{*}{C}H_2$	$R—C\equiv\overset{*}{C}H$	$R—\overset{*}{C}\equiv CH$	$R—CHO$	$R_2—CX_2$	$R—COOR'$	$COCl_2$
		CH_3NH_2	$R—CH_2NH_2$	Carbon	$R—CHX_2$		$R—CONH_2$	CX_4
		CH_3OH	RCH_2OH	R_2CHOH	$R—CH=NOH$		$R—CX_3$	H_2CO
		CH_3X	RCH_2X	$H—CHO$	$R—CH=N—R$		$R—CN$	CS_2
		$(CH_3)_3N$	$R—CH_2ONO_2$			CO	$R—COX$	
			RCH_2NO_2			CHX_3	$(RCO)_2—O$	
			RCH_2ONO			$HCOOH$		
		CH_3NO_2	$(RCH_2O)_2—SO_2$	CH_2X_2		$R—NC$		
			C_6H_6					

X = halogen throughout this paper.
Y = group joined through C (R, CH_3, COOH, COOR, CX_3, etc.).
Z = groups joined through N, O, S, or halogen (NO_2, OH, NH_2, SO_3H, Cl, etc.).

(*u*) $CaC_2 + 2H_2O \longrightarrow Ca(OH)_2 + CH\equiv CH$

(*v*) $Al_4C_3 + 12H_2O \longrightarrow 4Al(OH)_3 + 3CH_4$

The formulas of calcium carbide and aluminum carbide indicate that the valence of carbon is −1 and −4, respectively, and we see from equations (*u*) and (*v*) that these valences are so in acetylene and methane.

SUMMARY

A method is presented for balancing equations for organic oxidation-reduction reactions based on widespread concepts concerning the oxidation and reduction of organic compounds. The usual bonds found in organic compounds containing carbon, hydrogen, oxygen, nitrogen, sulfur, and the halogens are listed and the approximate formal charges on each atom from such bonds are indicated. The algebraic sum of the formal charges on an atom resulting from all of the bonds which that atom makes is called its polar number. The term "polar number" for elements in organic compounds, which is not original, is considered equivalent to the terms "oxidation state" or "valence" of elements in inorganic compounds. To balance an equation for an organic oxidation-reduction reaction, one determines the polar numbers of the atoms that undergo oxidation or reduction and applies the valence change or ion-electron methods of balancing redox equations. A number of examples are given.

Other authors have shown, and it is verified and further illustrated in this paper, that several classical organic reactions, such as halogenation, nitration, sulfonation, diazotization, Grignard formation, the Friedel-Crafts reaction, and molecular rearrangement, are oxidation-reduction reactions.

It is pointed out that primary, secondary, and tertiary carbon atoms are each of different oxidation levels.

LITERATURE CITED

(1) GREGG, D. C., THIS JOURNAL, **22**, 548 (1945).
(2) VANDERWERF, C. A., *ibid.*, **22**, 218 (1945).
(3) VANDERWERF, C. A., *ibid.*, **22**, 450 (1945).
(4) YOUNG, L. E., AND C. W. PORTER, "General Chemistry," Revised Ed., Prentice-Hall, Inc., New York, **1944**, pp. 267–8.
(5) CHERONIS, N. D., "Organic Chemistry," Thomas Y. Crowell Company, New York, **1943**, pp. 43–8.
(6) PAULING, L., "The Nature of the Chemical Bond," Cornell University Press, New York, **1940**.
(7) PORTER, C. W., "The Carbon Compounds," 2nd Revised Ed., Ginn and Company, New York, **1931**, pp. 4–8.
(8) WERTHEIM, E., "Organic Chemistry Laboratory Guide," The Blakiston Company, Philadelphia, **1937**, pp. 105–6.
(9) REMICK, A. E., "Electronic Interpretations of Organic Chemistry," John Wiley and Sons, Inc., New York, **1945**, pp. 47–52.
(10) FRY, H. S., "The Electronic Conception of Valence and the Constitution of Benzene," Longmans, Green and Company, New York, **1921**.
(11) HENRICK, F., translated by T. B. JOHNSON AND D. A. HAHN, "Theories of Organic Chemistry," Revised 4th German ed., John Wiley and Sons, Inc. New York, **1922**, pp. 111–2.
(12) NELSON, J. M., H. T. BEANS, AND K. G. FALK, *J. Am. Chem. Soc.*, **35**, 1810 (1913).
(13) BRAY, W. C., AND G. E. K. BRANCH, *ibid.*, **35**, 1440 (1913). McGAVOCK, W. C., "Organic Oxidation-Reduction Reactions," 2nd Ed., McGavock, San Antonio, **1945**.
(14) See for example, K. P. HANSEN, *Dansk Tids. Farm.*, **19**, 151–66 (1945); *Chem. Abs.*, **40**, 543 (1946); also paper presented before the Division of Chemical Education at the Detroit meeting of the American Chemical Society by ED. F. DEGERING as reported in *Abstracts of Papers*, 105th Meeting, American Chemical Society, Detroit Meeting, April 12–16, 1943, page 1D, Division of Chemical Education.

Patentability of Organic Compounds[1]

I. J. FELLNER
New York, New York

INVENTORS and their attorneys have allegedly met of late with some discouraging difficulties in obtaining adequate patent protection for organic compounds. From numerous objections raised against this type of invention they draw the conclusion that the Patent Office, its tribunals, and some Federal Courts have adopted a new, more rigid, and frequently even inconsistent standard in evaluating novelty and inventiveness of organic substances. The object of this paper is not an academic discussion on the soundness of the legal principles as applied and presented by the Patent Office, but rather a practical analysis of its more recent decisions and opinions by way of illustrations to guide us in a reasonable estimate of the value of patent applications with regard to their prospective allowance.

Organic compounds are patentably classified under the comprehensive term of "compositions of matter," but for the purpose of our study we will limit this term to the group of unitary structural entities of either a generic or a specifically defined configuration to the exclusion of physical mixtures or combinations in a chemically unreacted state. To be patentable, an organic compound must be new, inventive, and useful. Novelty and invention are interrelated criteria in that the height of the invention is measured by the state of the prior art. The gist of the invention may reside in the novelty of concept or of properties. Usefulness is an ancillary prerequisite and must be apparent and so indicated. Inherent or potential usefulness is not sufficient. The argument that every new organic compound, irrespective of its practical value, advances the art by enriching it with a new product is no longer accepted; therefore, claims for new chemical compounds will not be granted as a matter of course.

Among the manifold grounds of rejections employed by the Patent Office, the novelty of a compound is challenged because it represents merely an aggregation of known constituents or a substitution of groups within a homologous series of adjacent members whose configurative concept and chemical properties are easy to interpolate. In other cases rejections are based on a mere change of degree, lack of usefulness or unexpected qualities, or again on the ground of undue breadth of a claim.

One of the fundamental considerations in appraising inventive dignity of a chemical invention is the element of predictability, and modern practice frequently relies in this respect on the now almost classical rule of *In Re Wietzel*, or the "noninventive testing rule," (39 F (2), 669, 1930), where the following situation arose.

The applicant claimed a novel process of producing a mixture of formamide and hydrocyanic acid by treating an alkyl formate with ammonia in the presence of a dehydrating catalyst. The involved reaction may be illustrated by the following equations:

Patent

$$HCO{-}OR + NH_3 = ROH + HCO{-}NH_2$$
$$HCO{-}NH_2 \rightleftarrows HCN + H_2O$$

The prior art disclosed the preparation of higher amides and nitriles by treating higher aliphatic esters with ammonia, also in the presence of dehydrating agent, as represented by the following:

Reference

$$RCO{-}OR' + NH_3 = R'OH + RCO{-}NH_2$$
$$RCO{-}NH_2 \rightleftarrows RCN + H_2O$$

The Patent Office, considering hydrocyanic acid as the nitrile of formic acid, rejected the claims on the ground of close analogy between the two reactions. The applicant contended unpredictability of the claimed process in view of the fact that first members of a homologous series frequently display an atypical behavior with unforeseeable results and that this applied to formic acid as the head member of the fatty acid series. He further contested the hypothetical identification of hydrocyanic acid with the nitrile of formic acid. The Court of Customs and Patent Appeals, affirming the lower court of the Patent Office, formulated the following rule:

> And where there is no real reason to suppose that the result would not be produced, there is no invention in trying it and finding out that the process is successful.

This noninventive testing rule has been repeatedly quoted and interpreted and extensive comments thereon are found in the literature of Patent Jurisprudence.

An interesting case involving the issue of inventiveness in view of substitution is presented in the decision of *In Re Christmann* (43 USPQ 415, 1939). The invention related to an insecticidal composition including a reaction product of hydrofluosilicic acid and a guanidine. The basic guanidine constituent was intended to function as a repellent while the anionic hydrofluosilicic acid acted as toxic ingredient. The prior art showed (1) the mothproofing properties of guanidine compounds, (2) the mothproofing properties of guanidine plus fatty acids, (3) a wide variety of chemical reaction compounds of organic bases other than guanidine

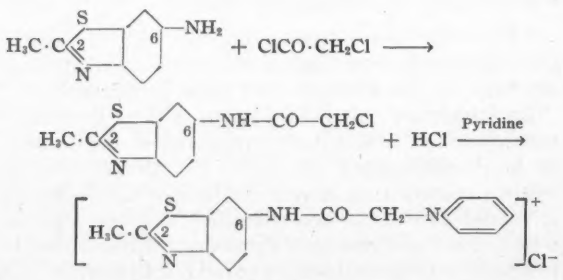
[1] Presented before the Division of Chemical Education at the 109th meeting of the American Chemical Society in Atlantic City, April 8–12, 1946.

with hydrofluosilicic acid, and (4) the insecticidal properties of fluosilicates.

During the litigation the question arose: Was it invention to substitute guanidine for the old organic bases in fluosilicate combinations? Was it inventive to substitute hydrofluosilicic acid for organic fatty acids in guanidine combinations? The Court of Customs and Patent Appeals said it was because the claimed compound was never conceived before and though guanidine, when standing alone, was known as having repelling qualities, no suggestion could be found in the prior art that it would retain such a characteristic when combined with hydrofluosilicic acid.

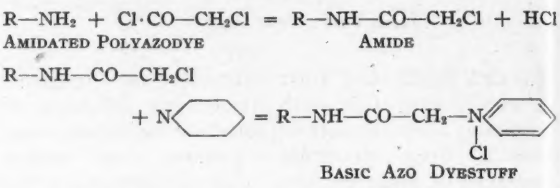
A similar situation was discussed in the case of *In Re de Groote* (53 USPQ 354, 1942) where a patent was sought for a reaction product of blown castor oil and diethanolamine. The reference disclosed (1) a compound consisting of *blown* castor oil and *tri*-ethanolamine, (2) a compound consisting of *unblown* castor oil and *di*-ethanolamine, and (3) a statement that commercial tri-ethanolamine ordinarily contains small amounts of di-ethanolamine. The Board of Appeals, referring to the aforementioned *Wietzel* doctrine, considered the claimed compound as a simple variation of features previously known which would suggestively fall within the skill of a chemist without involving new or unobvious results. The Board was reversed by the Court of Customs and Patent Appeals which rather followed the aforesaid decision of *Christmann* and made the important statement that the ruling of *Wietzel* is only applicable to process claims when the resulting product is old in the chemical art. Where, however, a new product is in issue, the prevision rule of *Wietzel* is not pertinent.

In *Ex parte Reister* (58 USPQ 620, 1942) the invention related to water-soluble heterocyclic compounds of the type used as starting materials for thiocyanine dyes. They were obtained by introducing into an amino-substituted derivative of a heterocyclic ring a quaternary ammonium group by means of an amino group. For the sake of clarity we will illustrate the invention by one embodiment of the generic formula as follows:

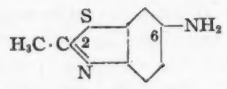


The compound is formed by treating 2-methyl-6-aminobenzothiazol with chloroacetylchloride whereby the chloroacetyl-2-methyl-benzothiazolamide(6) is obtained. The latter is then reacted with pyridine and yields the water-soluble quaternary ammonium thiocyanine of the configuration shown.

One reference showed the preparation of strongly basic azo dyestuffs by treating amidated polyazodyes successively with chloroacetylchloride and a tertiary heterocyclic base, as for instance,

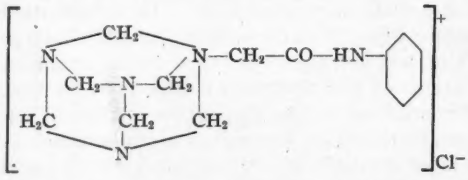


Another reference disclosed thiocyanins which had introduced into their molecules an amino group, as illustrated by the compound 2-methyl-6-amino-benzothiazol:

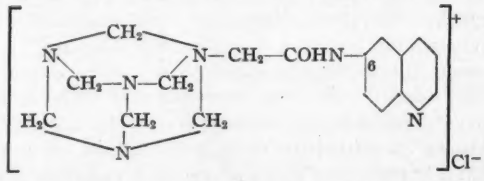


The examiner, in combining both references, concluded that it was obvious to replace R in R—NH_2 by the benzothiazol and to react it with chloroacetylchloride and subsequently with pyridine to arrive at applicant's configuration.

In another publication the examiner had found the disclosure of hexamethylenetetraminium salts formed of monohalogenated acetylated aromatic amines and hexamethylene-tetramine, as for example:



In a following example there was shown a reaction product resulting from the combination of 6-chloroacetyl-aminoquinoline and hexamethylene-tetramine.

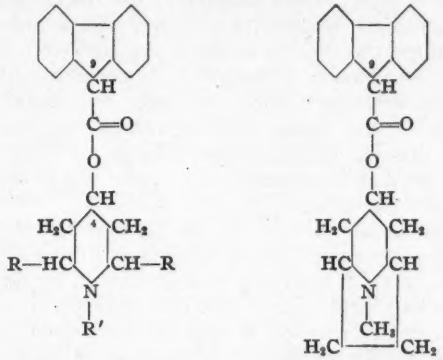


The examiner suggested that in this formula the hexamethylene group, being a tertiary amine, could apparently be substituted by a pyridine and that the quinoline was replaceable by any other known cyanine intermediate, such as the well-known 2-methyl-6-aminobenzothiazol. By this simple and allegedly obvious permutation of groups the applicant's formula could be conceived without the least inventive effort.

The Board of Appeals, reversing the examiner, ruled it to be inadmissible to pick out groups of unrelated molecular assemblages and to combine them for the

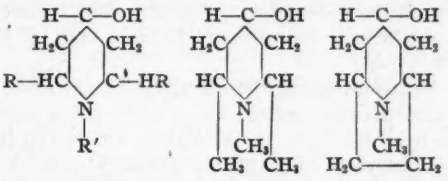
purpose of anticipating claims when none of the references suggests the regrouping as a useful feature in a particular type of compound. The decisive criterion for anticipatory transmutation, therefore, is whether the identity of each of the references is destroyed by reassembling their various groups to constitute the claimed compound. That this was done by the examiner in the instant case is evident.

A similar pattern is presented in the case of *Ex parte Burtner* (67 USPQ 185, 1944) where a patent was sought for antispasmodics in the form of basic esters of fluorene-9-carboxylic acid, as exemplified by a piperidinium-4-ol-ester of the following configuration:



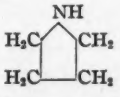
Patent *Reference*

The examiner stated that from a purely chemical standpoint the concept of the formula showed no patentable novelty over a French patent disclosing 9-fluorene-carboxylic acid esters of tropine and pseudotropine, such as illustrated. This statement was based



R-SUBSTITUTED 4-HYDROXYPIPERIDINOL OPEN-CHAIN TROPINE TROPINE

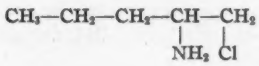
on the assumption, supported by Staudinger, that hydroxy-piperidinols may be considered as open-chain tropines if the pyrrolidine ring



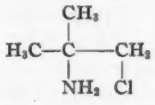
is disregarded. No invention was allegedly involved in substituting piperidin-4-ol for the tropines in the French patent. The examiner further contended that in view of the known medical value of tropines, the identical usefulness of the claimed and closely related piperidinol ester was suggestively revealed by the prior art. The Appellate Tribunal, however, though evading the controversial issue of configurative anticipation, allowed the use claim directed to antispasmodics in following the applicant's argument that in the field of drugs it is impossible to predict correctly the properties of chemical compounds without actual tests.

In cases of homologous relationship the prognosis for allowance of a compound claim is much less favorable. An illustrative example is furnished by *In Re Lincoln*, (53 USPQ 40, 1942) where a claim for 1-chloro-2-aminopentane was rejected on final appeal by the Court of Customs and Patent Appeals.

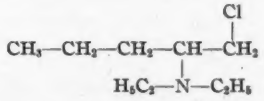
The controversial substance had the following formula:



The references were 1-chloro-2-amino-methylpropane, the next lower adjacent homolog,

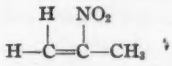


and 2-*N*-diethylamino-1-chloropentane,

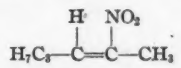


The court, in this case, decided that the compounds of the prior art differed from the claimed product only by the presence and the position of an alkyl group, while the reactive groups giving the compounds their characteristics are the same and similarly positioned. In the absence of unexpected properties there is no invention involved in the new compound, as novelty alone does not constitute invention.

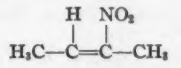
The identical fate was suffered by an application for nitro-olefins in the case of *In Re Hass and Susie*, (60 USPQ 544, 1944), where claims were drawn to 2-nitro-propene,



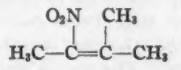
and 2-nitro-2-hexene



The claims were rejected over one reference disclosing mono-nitro-dimethyl-ethylene,



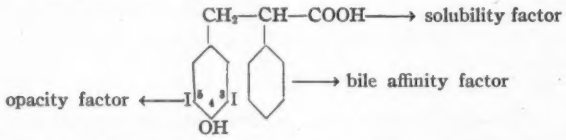
and nitro-trimethyl-ethylene,



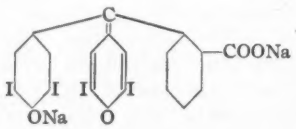
which is an isomer of 2-nitro-2-pentene.

The applicant contended that it ought not to be required to establish unexpected and unobvious properties or utilities not possessed by the previously known homologous and isomeric compounds. Claims to novel chemical products should be held to be patentable regardless of the prior art because such compounds tend substantially to promote the progress of science. The court, concurring with the examiner, pointed out that every chemist will recognize the same principal characteristics and physical properties in individual members varying from one to another in a homologous series and that the knowledge of the behavior of one of the members suggests to him the properties of the other members. It so confirmed the ruling of the prior decisions that novelty alone did not establish invention.

These two cases should be carefully compared with a recent decision rendered by the second Circuit Court of Appeals in *Schering Corporation vs. Gilbert*, (68 USPQ 84, 1946). In this infringement suit a patent to *Schering* relating to poly-iodized derivatives of hydroxy-diphenylcarboxylic acids was attacked for lack of novelty. The litigious claim was drawn to *beta*-(4-hydroxy-3,5-di-iodophenyl)-*alpha*-phenyl-propionic acid of the following configuration:



and the usefulness of the compound resided in its application as contrast medium in cholecystographic combinations where tetra-iodo-phenolphthalein was used theretofore:



The patentee relied on the advantageous combination of the solubility factor of the carboxylic group with the bile affinity of the phenyl component and the opacity of the iodine and referred to the harmful after-effects of toxicity in the phenolphthalein diagnosis. The defendant contended that the concept of the formula was predictable as a result of inevitable chemical reactions governed by the law of nature and that there was no novelty in the process used to produce that result.

The court admitted the seemingly slight departure from the prior art structure, but emphasized that novelty and inventiveness must be evaluated not alone by the degree of change, but also in the light of the purpose sought to be accomplished. The particular configuration of the new molecule is but one of the millions of possible permutations in the rearrangement of atoms in the benzene ring. To elect the one that would impart to the new molecule the attributes which make it so uniquely acceptable as a contrast agent is sufficient evidence for inventiveness to support the validity of the claim. The interesting implication of this decision is that a new, though not inventive, compound may be patentable in view of its unexpected properties and utilities.

In conclusion we may tentatively state the following rules governing the patentability of organic compounds: (1) If the compound is novel in its concept and/or its characteristics and unpredictable as to its possibility of existence, it may be patentable *per se*, and utility is an ancillary prerequisite of its patentability. (2) If the compound is new but not inventive in concept in view of isomeric or homologous relationship with prior art compounds, inventiveness may be supported by unexpected useful properties. (3) If the compound is old and claimed only for a new and useful application, it generally does not qualify as a patentable invention unless it is adapted in some manner for the new purpose. This rule has been established in the recent decision of *In Re Thuau* (57 USPQ 324, 1943).

The apparent change of standards in the evaluation of inventiveness of organic compounds is not based on new judicial doctrines of the Patent Office and its tribunals, but rather constitutes a natural result of our more refined discernment as reflected by the rapid advance of the science of chemistry.

There's a possibility that important developments may be achieved in medical research on brain diseases through the discovery of a novel use for malachite green. When a solution of this green dye is injected into the brain, it turns any diseased tissues green so that they are readily distinguishable from normal tissues, which retain their natural color. The dye is harmless and disappears within three days.—Dyelines and Bylines (July, 1946).

THE POSITIVE CHARACTER of the HALOGENS

JACOB KLEINBERG

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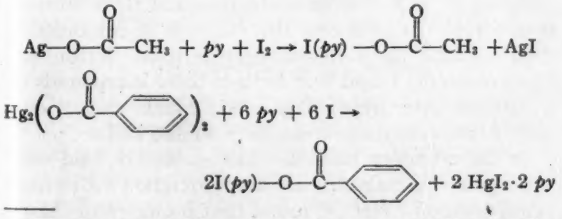
THE student in general chemistry is taught that the halogens are typical nonmetals and that their ability to form inorganic compounds depends upon the ease with which they pick up an electron to complete their outermost orbits. The electronegativity of these elements is continually stressed, and it is pointed out that the chlorine atom, having the greatest affinity for electrons, can displace bromine and iodine from solutions of their salts. Insufficient emphasis is placed on the fact that this is true only when the halogens are acting as negative elements. Little or no mention is made of the fact that in the oxyhalogen compounds, the reverse is true—namely, that iodine will replace chlorine from potassium chlorate or bromine from potassium bromate.

The discovery in recent years that iodine and bromine may form coordination compounds with organic bases, such as pyridine, in which they act as positive univalent ions, will undoubtedly initiate new investigations. Therefore, a discussion of some of the aspects of the positive character of the halogens is in order.

COORDINATION COMPOUNDS OF POSITIVE UNIVALENT IODINE AND BROMINE

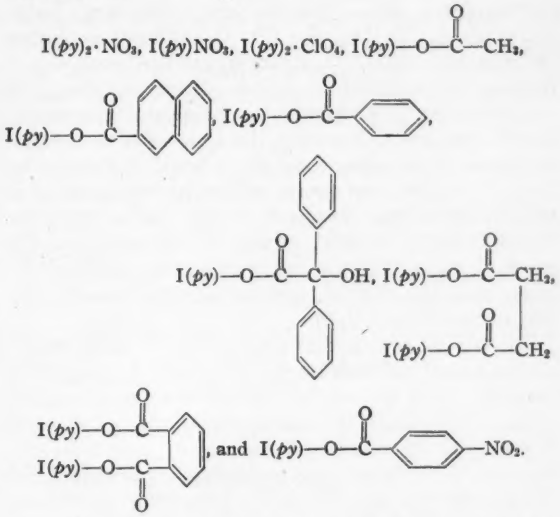
The suggestion of Cofman (*1*) that hypoiodous acid may have the properties of a very labile base, IOH, is brilliantly substantiated by the investigations of Carlsohn and his students (*2, 3, 4*). Reasoning that IOH might be stabilized by coordination with pyridine (*py*), these investigators succeeded in preparing a series of salts of the hypothetical bases $I(py)OH$* and $I(py)_2OH$. From their behavior, there is no doubt that the iodine exists in a positive univalent state in these compounds.

The salts are generally prepared by treating the silver salt or the mercurous salt of the necessary acid with the calculated amount of iodine and a slight excess of pyridine in some nonaqueous solvent such as chloroform. Reaction occurs immediately according to the equations



* The $I \cdot py^+$ ion has been postulated to account in part for the conductivity of iodine in pyridine [Audrieth and Birr, *J. Am. Chem. Soc.*, 55, 668 (1933)].

The following were prepared as definite crystalline compounds:



The chemical reactions of these salts show that the iodine is positive and univalent. When dissolved in sodium hydroxide containing potassium iodide and then acidified, they all liberate free iodine.

$$I^+ + I^- \rightarrow I_2$$

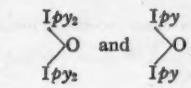
This reaction is utilized for the determination of iodine in the compounds. With potassium chloride and potassium bromide a double decomposition takes place with the formation of $ICl \cdot py$ and $IBr \cdot py$, respectively.

The iodi-pyridine salts hydrolyze slowly in water in accordance with the following equations:

$$I(py)_2 \cdot NO_3 + HOH \rightarrow I(py)OH + pyH \cdot NO_3$$
$$5\ I(py)OH \rightarrow 2\ I_2 + pyHIO_3 + 2\ HOH + 4\ py$$

Iodi-pyridine salts react immediately with an acidic phenol solution to form iodophenol. Cofman (*1*) has presented evidence to indicate that iodination of phenol is accomplished only by positive univalent iodine and not by the iodate ion, free iodine, nor by the iodide ion.

By treatment with sodium hydroxide solution the bases $I(py)_2 \cdot OH$ and $Ipy \cdot OH$ are liberated. These immediately go over to their respective anhydrides,



which may be isolated. This indicates that

the anhydride of IOH, can be stabilized by coordination with pyridine.

On the basis of the decomposition potentials of ICl, IBr, and ICl_3, and electrode potential measurements of the iodine electrode against solutions of the above substances, Finkelstein (*5*) has demonstrated that the I^+ ion should be placed with the noble metals in the electromotive series. This was substantiated in a qualitative manner by Carlsohn (*2*). A chloroform solution of dipyridine iodine (I) nitrate was treated with metallic zinc, magnesium, iron, copper, silver, mercury, gold, and platinum. All replaced the iodine and were immediately dissolved. However, it is impossible to say that iodine is more noble than silver since dipyridine iodine (I) nitrate was prepared by the replacement of silver with iodine. Evidently in the case of silver the reaction can go in both directions. In each case the insoluble silver iodide formed removes the replaced element from the reaction, and perhaps this accounts for the apparent reversibility.

Electrolysis of dipyridine iodine (I) nitrate in water-pyridine and methanol solutions yields iodine at the cathode, while the solution around the anode remains clear. However, it is entirely possible that the iodine is deposited at the cathode because of a secondary reduction. To rule out this possibility, dipyridine iodine (I) nitrate was electrolyzed in anhydrous chloroform, and here again iodine was precipitated at the cathode. This proves beyond doubt that the iodine is the positive constituent of the salt.

Assuming a coordination number of two for positive univalent iodine, Carlsohn postulated the following types of structure for the salts: $[I(py)_2]X$ and $[I\overset{py}{X}]$ (X = acid radical). An attempt was made to verify these structures by conductivity measurements. Salts of the type $[I(py)_2]X$ should be good conductors, whereas those of type $[I\overset{py}{X}]$ should not conduct the electric current. Moreover, salts of the latter type should revert to the form $[I(py)_2]X$ in pyridine solution according to the equation $[I\overset{py}{X}] \rightleftarrows [I(py)_2]\,X$ and thus should become conductors.

The results of the conductivity experiments are given in Tables 1 and 2.

From Table 1 it is apparent that although $Ipy\cdot NO_3$ has a small equivalent conductance in acetone in comparison with $I(py)_2NO_3$, it still conducts the current appreciably. Carlsohn makes no explanation for this phenomenon. It is possible that acetone enters the coordination sphere to some extent and forms a coordinate covalent bond with the iodine by means of a free pair of electrons on the carbonyl oxygen. This would drive nitrate ion out of the coordination sphere and thus make the compound a conductor. The data in Table 2 lend credence to such a mechanism. Monopyridine iodine (I) nitrate conducts the current in methanol equally well whether or not pyridine is present, whereas the conductivity of the benzoate is increased tremendously by the addition of pyridine. It should be borne in mind that the nitrate ion is an extremely electronegative unit and it would therefore exhibit a lesser tendency to form a coordination bond than the benzoate ion. In the case of the nitrate, methanol may well coordinate to the positive iodine through a free pair of electrons on the oxygen. On the whole the conductivity measurements leave considerable doubt concerning the coordination number of positive univalent iodine.

Salts in which methyl-substituted pyridines have been coordinated to positive univalent iodine have also been prepared by Carlsohn (*3*). These are $[I(\beta\text{-picoline})_2]NO_3$, $[I(2,6\text{-lutidine})_2]NO_3$, $I(2,4\text{-lutidine})_2NO_3$, and $[I(2,4,6\text{-collidine})_{3½}]NO_3$.

The corresponding compounds containing positive bromine, $[Br(py)_2]NO_3$ and $[Br(py)_2]ClO_4$, have also been prepared by Carlsohn (*4*) by methods similar to those used for the preparation of the iodine salts; the former was first prepared by Uschakov and Tchistov (*6*). The method of analysis of these compounds demonstrates that the bromine is positive. A sample of a bromi-pyridine salt is treated with potassium iodide dissolved in sodium hydroxide, the solution acidified with sulfuric acid, and the liberated iodine is titrated with sodium thiosulfate. One atom of bromine liberates two of iodine.

$$(Br^+ + 2I^- \rightarrow Br^- + I_2)$$

TABLE 1

EQUIVALENT CONDUCTANCE OF IODI-PYRIDINE SALTS IN ACETONE AT 20°C.

Dilution	*Salt*	*Ohm^{-1} cm.^{2}*
V = 100	$I(py)_2NO_3$	41·6
	$Ipy\cdot NO_3$	13
	$Ipy\cdot OOC\cdot CH_3$	0·06
	$Ipy\cdot OOC\cdot C_6H_5$	0·06
V = 200	$Ipy\cdot OOC\cdot CH_3$ | $Ipy\cdot OOC\cdot CH_3$	1.7

TABLE 2

EQUIVALENT CONDUCTANCE OF IODI-PYRIDINE SALTS IN METHANOL AT 20°C.

Dilution	*Salt*	*Ohm^{-1} cm.^{2}*
V = 100	$Ipy\cdot NO_3$	55.3
	$Ipy\cdot NO_3$ + about two mols of pyridine	55.3
	$Ipy\cdot OOC\cdot C_6H_5$	2
	$Ipy\cdot OOC\cdot C_6H_5$ + about two mols of pyridine	15.2

THE ELECTROLYSIS OF THE CYANOGEN HALIDES

There is excellent evidence that the iodine in such compounds as iodine monochloride and monobromide is positive. In each case the iodine is in combination with a much more electronegative unit. Orton and Blackmann (*7*) found that both of these compounds on hydrolysis give hypoiodous acid, which undergoes a self oxidation-reduction to iodic acid and iodine.

In the cyanogen halides—chloro-, bromo-, and iodocyanogen—the halogens are in combination with a halogen-like group. Nef (*8*) found that bromo- and chlorocyanogen yielded potassium bromide and chloride, respectively, when boiled with potassium hydroxide,

whereas iodocyanogen formed potassium iodate and iodide. From this one might infer that the bromine and chlorine were negative in these compounds while the iodine was positive. It has also been shown (*9*) from the action of hydrohalic acids on iodocyanogen that the iodine has a positive character. The reactions cited above may be summarized in a series of equations.

$$\overset{-}{\mathrm{Br}}\overset{+}{\mathrm{CN}} + 2\,\mathrm{KOH} \rightarrow \mathrm{KOCN} + \mathrm{KBr} + \mathrm{H_2O}\dagger \quad (1)$$

$$\overset{-}{\mathrm{Cl}}\overset{+}{\mathrm{CN}} + 2\,\mathrm{KOH} \rightarrow \mathrm{KOCN} + \mathrm{KCl} + \mathrm{H_2O} \quad (2)$$

$$\overset{+}{\mathrm{I}}\overset{-}{\mathrm{CN}} + 2\,\mathrm{KOH} \rightarrow \mathrm{KCN} + \mathrm{KOI} + \mathrm{H_2O}$$
$$3\,\mathrm{KOI} \rightarrow \mathrm{KIO_3} + 2\,\mathrm{KI} \quad (3)$$

$$\overset{+}{\mathrm{I}}\overset{-}{\mathrm{CN}} + \mathrm{HCl} \rightarrow \mathrm{HCN} + \overset{+}{\mathrm{I}}\overset{-}{\mathrm{Cl}} \quad (4)$$

Clark and Streight (*10*) studied the electrolysis of the cyanogen halides in various solvents. From Nef's work on the hydrolysis of the cyanogen halides one might have expected that the iodine in iodocyanogen would migrate to the cathode in all solvents. Such, however, is not the case. As is seen from Table 3, only in pyridine does the iodine react electronegatively.

TABLE 3

THE ELECTROLYSIS OF CYANOGEN HALIDES BETWEEN SILVER ELECTRODES AT ROOM TEMPERATURE

Solute	*Solvent*	*Anode deposit*	*Cathode deposit*
BrCN	Acetonitrile	Bromide	Cyanide
	Nitrobenzene	Bromide	Cyanide
	Methanol	Bromide	Cyanide
	Ethylene glycol	Bromide	Cyanide
	Furan	Nonconductor	
	Pyridine	Tarry precipitate	
	Aniline	Bromide	Cyanogen gas
ICN	Benzene	Iodide	Cyanide
	Acetonitrile	Iodide	Cyanide
	Nitrobenzene	Iodide	Cyanide
	Methanol	Iodide	Cyanide
	Ethanol	Iodide	Cyanide
	Nitromethane	Iodide	Cyanide
	Pyridine	Cyanide	Iodide
	Aniline	Iodide	Cyanogen gas and paracyanogen
	Quinoline	Iodide	...
	Pyrrol	Reacted chemically	

Cyanogen iodide seems to behave as an electromer, that is, it may ionize reversibly as follows:

$$\overset{+}{\mathrm{I}}\cdot\overset{-}{\mathrm{CN}} \rightleftharpoons \overset{-}{\mathrm{I}}\cdot\overset{+}{\mathrm{CN}}$$

Clark and Streight found that there is no direct correlation between the concentration of the two electromers present in solution and the dielectric constant of the solvent. However, it is apparent here, as in other examples involving positive halogen, that the solvent plays an important and as yet undetermined role.

POSITIVE TRIVALENT IODINE

There is considerable evidence that iodine may also exist as a trivalent cation. Partington and Bahl investigated the action of oxidizing agents on elementary iodine and confirmed the observation that ozonized oxygen will convert iodine to a compound having the formula I_4O_9 (*11*). These workers considered this substance to be the normal iodate of trivalent positive iodine, $I(IO_3)_3$. The same compound has also been prepared by the treatment of iodic acid with phosphoric acid (*12*). The basic iodate, $IO(IO_3)$, is produced by the action of hot, concentrated sulfuric acid on iodic acid, followed by treatment of the product formed with water (*11*). The oxidation of iodine by perchloric acid or by ozone and perchloric acid gives rise to the formation of a perchlorate, the composition of which may be represented by the formula $I(ClO_4)_3 \cdot 2H_2O$ (*13*). The normal sulfate, $I_2(SO_4)_3$, is formed when the basic sulfate is treated with sulfur trioxide at 100–120°C.

Fouque (*14*) first discovered that fuming nitric acid will oxidize iodine in the presence of acetic anhydride to the normal triacetate, $I(OOCCH_3)_3$. Fichter and Stern (*13*) utilized this reaction to prepare a whole series of compounds of trivalent iodine. The results are summarized in Table 4.

TABLE 4

SOME COMPOUNDS OF POSITIVE TRIVALENT IODINE

Compound	*Method of preparation*
IPO	$I_2 + H_3PO_4 + (CH_3CO)_2O$ + concentrated HNO_3
$I(COOCCl_3)_3$	$I_2 + CCl_3COOH + (CH_3CO)_2O$ + fuming HNO_3
$I(COOCHCl_2)_3$	$I_2 + CHCl_2COOH + (CH_3CO)_2O$ + fuming HNO_3
$I(COOCH_2Cl)_3$	$I_2 + CH_2ClCOOH + (CH_3CO)_2O$ + fuming HNO_3
$I(COOCH_2Br)_3 \cdot I(IO_3)_3$	$I_2 + CH_2BrCOOH + (CH_3CO)_2O$ + fuming HNO_3
$I(SO_2CH_3)_3$	$I(COOCH_3)_3 + CH_3SO_3H$
$I(COCCl_3)_3 \cdot I(IO_3)_3$	$I_2 + CCl_3COOH + O_3$

These compounds are sensitive to moisture and quite unstable to heat. They hydrolyze readily in accordance with the following equation:

$$5\,\mathrm{IPO_4} + 9\,\mathrm{H_2O} \rightarrow \mathrm{I_2} + 3\,\mathrm{HIO_3} + 5\,\mathrm{H_3PO_4}$$

The fact that the iodine in the compounds described above exists in a positive trivalent state has been strikingly demonstrated by Fichter and Stern (*13*). When a saturated solution of iodine triacetate in acetic anhydride is electrolyzed, iodine is deposited on the cathode in direct concordance with Faraday's Laws.

Positive trivalent iodine may also exist as part of the anion in polyhalide complexes. The acid, $HICl_4 \cdot 4H_2O$, is obtained when iodine, suspended in concentrated hydrochloric acid, is treated with chlorine (*15*). The salts, $KICl_4$, $RbICl_4$, $CsICl_4$, and $Mg(ICl_4)_2 \cdot 8H_2O$ may also be prepared. It has been shown (*16*, *17*, *18*) that the ICl_4^- ion is one of the more stable of the polyhalide anions, and this stability is attributed to the fact that iodine (a large electropositive ion) is surrounded by chlorine atoms (small electronegative atoms).

† The charges shown indicate polarity.

LITERATURE CITED

(1) COFMAN, V., *J. Chem. Soc.*, **115**, 1040 (1919).
(2) CARLSOHN, H., "Uber Eine Neue Klasse Von Verbindungen des Positiv Einwertigen Iods," Verlag Hirzel, Leipzig, **1932**.
(3) CARLSOHN, H., *Angew. Chem.*, **46**, 747 (1933).
(4) CARLSOHN, H., *Ber.*, **68**, 2209 (1935).
(5) FINKELSTEIN, V., *Z. physik. Chem.*, **124**, 285 (1926).
(6) USCHAKOV, M. I., AND W. O. TCHISTOV, *Ber.*, **68**, 824 (1935).
(7) ORTON, K. J., AND W. L. BLACKMANN, *J. Chem. Soc.*, **77**, 830 (1900).

(8) NEF, J. U., *Ann.*, **287**, 265 (1895).
(9) CHATTAWAY, F. D., AND J. M. WADMORE, *J. Chem. Soc.*, **81**, 191 (1902).
(10) CLARK, R. H., AND H. R. L. STREIGHT, *Trans. Roy. Soc. Canada* [3], **22**, 323 (1928).
(11) PARTINGTON, J. R., AND R. K. BAHL, *J. Chem. Soc.*, 1258 (1935).
(12) FICHTER, F., AND H. KAPPELER, *Z. anorg. Chem.*, **91**, 134 (1915).
(13) FICHTER, F., AND S. STERN, *Helv. Chim. Acta*, **11**, 1256 (1928).
(14) FOUQUE, G., *Chem. Ztg.*, **38**, 680 (1914).
(15) EMELÉUS, H. S., AND J. S. ANDERSON, "Modern Aspects of Inorganic Chemistry," D. Van Nostrand Company, Inc., New York, **1939**, p. 331.
(16) CREMER, H. W., AND D. R. DUNCAN, *J. Chem. Soc.*, 2243 (1936).
(17) CREMER, H. W., AND D. R. DUNCAN, *ibid.*, 181 (1933).
(18) READE, T. H., *ibid.*, 2528 (1926).

Here and There in the Trade Literature

IT WOULD be too bad to miss any of the numbers of the *Interchemical Review*, especially the Spring, 1946, with food for the organic chemist in the form of "Synthetic amino acids," as well as a good elementary "Brief review of atomic physics."

● "Power from atoms: How soon?" is a question discussed ably by E. V. Murphree in the June *Lamp*. There is also to found in the same number an article on new types of insecticides.

● An interesting article in the June *Socony-Vacuum News* pictures some of the war damage done to refineries in Germany. The author, Mr. L. P. Evans, reports that:

> . . . the opinion of the German oil people is that Germany lost the war because of the crippling effect of intensified air raids on transportation facilities and synthetic gasoline plants. This resulted in almost complete stoppage of aviation gasoline production and the subsequent grounding of the Luftwaffe. Statistics on Germany's aviation gasoline production seized in Hamburg indicated that beginning early in 1944, as a result of the intensified bombardment from the sky, the daily country-wide production of aviation gasoline diminished to the vanishing point by the first week of September of that year. It never regained sufficiently to be of consequence.

● Expansion of the petroleum industry into the general organic chemical field is a recent development. The *Lion Oil News* for June describes how one company is making this transition. There are some excellent pictures of the manufacture of ammonia and its various products by the latest methods.

● "Oxycel" is a new product of some chemical interest described in the June *Therapeutic Notes:*

> Surgeons have long appreciated the need for an absorbable, nonirritating, hemostatic, gauze-like material that could be safely left in the tissues at operation. Oxycel fills this need.
>
> Oxycel is not surgical gauze; it is not a cotton surgical dressing. Oxycel is an entirely new addition to the surgical armamentarium; an absorbable, gauze-like and cotton-like material that significantly facilitates hemostasis. Routine use of Oxycel is obviously advantageous in general surgery and all specialized branches of surgical practice.
>
> Oxycel which is absorbable, hemostatic, oxidized cellulose is a creation of organic chemistry; it is unique both in its freedom from irritating properties and its capacity to absorb from body tissues. Applied as a tampon or packing to oozing serous membranes or bleeding organs and tissues in any part of the body, it can be left *in situ* with practically no danger of clinically significant scar formation or inflammatory reaction in the tissues.

● Not altogether chemical, but fascinating nevertheless, is a piece in the July *Merck Report* entitled "Primitive medicine: A contrast with modern practice." To keep up with important developments one should also read "Peacetime implications of biological warfare" by George W. Merck, who was chairman of the United States Biological Warfare Committee.

● Some facts about present-day gasoline, said to be "stranger than fiction," are to be found in an article in the July *Service*. The requirements and specifications of an ideal motor fuel are discussed, along with the extent to which they are met by today's gasolines. An extensive Supplement to this number recounts in considerable detail how one oil company "went to war." It is a good addition to the already extensive literature describing how America's "Industrial Might" defended the freedoms which created it.

● *Dyestuffs* completes its two-installment series on "Antiseptic properties of surface-active agents" in the Spring, 1946, issue ending in a summary:

> Soap has always been and still is a valuable antiseptic agent. Among the new synthetic detergents, products are available which can be used in neutral or acid solutions to give a much stronger antiseptic action than is possible with soap solutions. These new detergents are valuable because a really worth-while antiseptic action is obtained from products which are not toxic. The new detergents are nonvolatile so that they are stable under storage conditions, and they dissolve rapidly to start their sterilizing action.

● The June number of the *Imperial Oil Review* contains several items of interest: the announcement of a scholarship plan establishing 11 undergraduate scholarships, of $500 each, to be awarded for study at any Canadian university; an article on synthetic power, which has nothing to do with atomoclastic energy but rather with synthetic hydrocarbon fuels; an account of the "Search unending," for new sources of petroleum; and a nice account of the technical production of plastics from petroleum.

● The *Dow Diamond* for July is loaded with magnesium. "The bright magnesium picture" is painted in some detail, principally devoted to present and future uses. Elsewhere, a 75-pound magnesium boat is pictured and described, which makes one want to start immediately on a camping trip with one of these over his shoulder.

• The *Dupont Magazine* for August–September adds to the trade literature on insecticides with an article on freon and another, "DDT, yesterday and today."

• And concerning penicillin, we quote the following from the May *What's New:*

WHAT DO YOU MEAN, "PENICILLIN?"

Medical editors all over the land have been groaning expressively for more than a year now whenever they hear or read the word "penicillin." If they published every paper sent to them about this new discovery, they affirm, they would have space for nothing else. Everybody has something to say or write about "penicillin," and it seems certain that any man would be considered just a little odd if he ventured to ask: "What do you mean by 'penicillin?' "

The fact is, however, that few who speak or write about penicillin are in a position to define precisely what they mean by the term. The fact that penicillin is a complex and variable mixture of substances having vitally different therapeutic and physiological properties is just beginning to be appreciated. That these properties may drastically influence the therapeutic response of different diseases to the drug has only recently become evident. It seems, therefore, worthwhile to consider just what is meant by the word "penicillin," and thereafter to be guided in using it by the fuller understanding which chemical science can give.

Penicillin was the name given in 1929 by Alexander Fleming to the active principle produced by the growth, on a specified medium, of a mold subsequently identified as a strain of *Penicillium notatum.* This principle inhibited the growth of *Staphylococcus aureus* and other gram-positive bacteria. Fleming did not isolate penicillin or in any way characterize the substance from the chemical point of view.

In 1943, using another strain of *P. notatum* and a different medium for its growth, American workers first isolated pure crystalline penicillin. Two months later, English workers succeeded in isolating the pure principle as produced by Fleming. It soon developed that the American and English "penicillins" were two different (though very closely related) chemical compounds. These are now known in this country as penicillins G and F, respectively—in England as penicillins II and I. In 1944 a third penicillin (X or III) was isolated and identified, and in 1945 still a fourth (K or IV). Other members of the penicillin family are known, but, from the commercial and clinical points of view, only these four, penicillins F, G, K, and X, are presently of importance.

For those who are chemically minded, each of these four penicillins has the same basic structure—but with a different side chain corresponding to each of the penicillins. For penicillin G, this side chain is a benzyl group. The substance penicillin X has a para-hydroxybenzyl group, while F and K are both found to be aliphatic, being characterized by the Δ^2-pentenyl and *n*-hepytl groups, respectively.

The penicillin available on the market is made by a dozen or more producers, with various strains of mold, growth conditions, media, and recovery processes being used. The result is that what is labeled as "penicillin" may contain, in varying amounts, a variety of active principles as well as their associated (but inert) impurities. Even should a label indicate the potency in terms of units per milligram, it is no criterion of purity, inasmuch as the pure penicillins range from 900 to 2300 units per milligram. Hence, pure penicillin X would show the same potency in units per milligram as a sample of K which contained 61 per cent of inert impurities.

So much for purity. What about the variety of penicillin? Is 100,000 units of penicillin G of greater or less value than the same number of units of F, K, or X? Unfortunately, the answer to this question is known only in part. It depends on many factors, such as their relative activity against the gamut of organisms which the clinician wishes to counteract, and on their relative stabilities and rates of excretion.

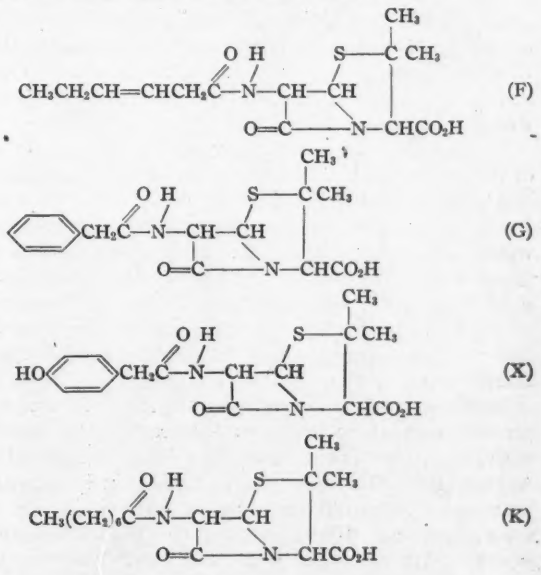
The first of these problems, the relative activities against a variety of pathogenic organisms, is very complicated. For instance, there are strains of staphylococcus which are extremely sensitive to penicillin—others which are quite resistant. It almost becomes a matter of having to determine the sensitivity of each isolate to each of the various penicillins, obviously a task of infinite proportions. However, in time, it is hoped that certain generalizations may become evident.

With reference to the relative rates of excretion and destruction of the various penicillins, recent experiments of Abbott workers (using themselves as guinea pigs) have thrown much light on the subject. These results have been confirmed in other laboratories. It appears from this work that there is no appreciable difference in the rates at which the different penicillins are excreted—they are all disconcertingly fast. An unexpected observation, however, was that penicillin K is very rapidly destroyed in the body. When 25,000 units of each of three pure crystalline penicillins (G, X, and K) were injected intravenously, satisfactory blood levels (against a hemolytic streptococcus) of 0.03 unit per cc. were maintained for roughly one-half, two, and four hours for penicillins K, G, and X, respectively. The four-hour level for penicillin X is unduly exaggerated because the hemolytic streptococcus is much more sensitive to this penicillin than to G or K. The urinary excretion was also measured, and it was observed that whereas penicillins G and X were excreted to the extent of 70 to 75 per cent in two hours, less than 30 per cent of penicillin K was excreted. Obviously, penicillin K was being destroyed in the body almost faster than it could be excreted—fast as that is. This explains why satisfactory blood levels of K are so fleeting.

In view of this unsatisfactory action of penicillin K in the body, a 100,000-unit bottle of this penicillin would obviously not have the same value in combating infections as 100,000-unit bottles of penicillins G or X, and one can only recommend that penicillins high in K not be used. After this principle had been established, Abbott chemists, not without trepidation, made a laborious analysis of a current commercial lot. Greatly to their relief and satisfaction it was found that their product contained not more than 8 per cent of penicillin K.

The day is undoubtedly coming when physicians will wish to prescribe a specific penicillin for a given condition. That day, however, must await the development of better methods of determining the proportions of the various penicillins in a given product, better methods for their production and separation, and a more exact knowledge of which ones we wish to use. The pharmaceutical industry is fully cognizant of the importance of these problems and can be counted upon to give those problems its early and earnest attention.

The formulas for the four penicillins are given as:



Out of the Editor's Basket

THE relationship between Allied strategy during World War II and the volume of American industrial production is shown strikingly in a historical report, "Chronology of the War Production Board and Predecessor Agencies: August, 1939, to November, 1945," issued by the Civilian Production Administration, successor to the WPB.

Analysis of industrial production as the war progressed underlines the fact that the decision of Allied strategists to fight two wars simultaneously in widely separated areas was made possible only by the record-breaking efforts of American industry and labor.

Designed for use as a reference aid by editors, educators, librarians, historians, and students of American economic history, the report relates chronologically (1) the major military and diplomatic events of the war, (2) the industrial problems, such as the need for controls and priorities, labor shortages, and planning for reconversion, which stemmed from the war situation, and (3) the action taken by the War Production Board and predecessor agencies to eliminate supply bottlenecks and increase production to meet the strategic needs of the war.

A chronological chart accompanying the detailed report summarizes the military highlights of the war in relation to problems of industrial mobilization and production. It reveals that American defense production really got under way only after the German conquest of Poland in September, 1939, and developed gradually in 1940 and 1941. After the confusion resulting from Pearl Harbor had disappeared, production for war increased sharply and expanded greatly again during 1942 when the Japanese advance in the Pacific was checked at Guadalcanal in August, and the Allies invaded North Africa in November of that year.

During 1943 victories at Stalingrad and in the Battle of the Atlantic, the Allied invasions of Sicily and Italy, and the capture of the Aleutians and Tarawa from the Japanese brought increased demands for supplies from widely separated battlefronts. Production reached its peak in November, 1943, and remained at a high level until May, 1945, when after the victory in Europe it dropped precipitately. Not until the defeat of Japan, however, did war production drop to its pre-Pearl Harbor level.

Beginning with the early period of American defense preparedness which President Roosevelt set in motion with the establishment of the War Resources Board in August, 1939, the report outlines the principal contributions to industrial mobilization and production of several agencies which preceded the War Production Board. Among these were the Inter-departmental Committee for Coordination of Foreign and Domestic Military Purchases (December, 1939, to April, 1941), Office for Emergency Management (May, 1940), Advisory Commission to the Council of Na ional Defense (May to December, 1940), Office of Production Management (January to December, 1941), and the Supply Priorities and Allocations Board (August, 1941, to January, 1942).

The War Production Board, established on January 16, 1942, continued until November 4, 1945, when the Civilian Production Administration was set up to facilitate the reconversion of industry from war to civilian production.

Basis for College Recruiting

The following statement by Dr. Fred J. Kelly, in *Higher Education*, will be of interest to all who are in any way concerned with future college enrollments:

> In 1900 the pupils in public high schools (last four grades) reporting to the U. S. Office of Education numbered 519,251. By 1920 the number reached 2,200,389. By 1940 it reached 6,601,444. In some states the high schools enroll nearly all the youth of high-school age. For the country as a whole about 75 per cent of those of high-school ages are enrolled in high schools, and a little more than half the young people graduate from high school before they discontinue attendance permanently.
>
> How much higher will that graduation percentage go? With all the "ifs" in mind it seems reasonable to expect the increase to continue, but the numbers of young people graduating from high school will level off at around 75 to 85 per cent, at which time we shall have an annual high-school graduating class of about 1,600,000 to 1,800,000. In the 1950's there will be an appreciable effect in the high schools as a result of the decreased birth rate, which has cut down elementary school enrollments in recent years.
>
> This means that the high-school graduates upon whom we may draw for college enrollments will increase by perhaps 50 per cent, but we shall soon experience a decline in the rate of increase and will approach a relatively stable figure. However, for the next decade the numbers will continue to increase. Furthermore, the changing attitude of many of the colleges, particularly publicly supported ones, toward less selective admission will provide in colleges for practically a cross section of this increased number. It seems reasonable, therefore, that the upward trend to 1,625,000 college students by 1950 coming regularly from the high schools will not be seriously affected by the change of trend in high-school graduates.

Stream Pollution Picture

"Clean Waters," a new 16-mm. color and sound motion picture produced by the General Electric Company in cooperation with the United States Public Health Service, is now available for showings to civic organizations and other interested groups throughout the country. With scenes of pictorial beauty, the film emphasizes the importance of clean waters as an essential natural resource. Then in contrast the effects of water pollution are shown: the destruction of wild life and recreational facilities, the deterioration of waterfront property, the spread of waterborne diseases, such as typhoid fever, cholera, and dysentery. U. S. Public Health Service figures point out that pollution of waters

costs the nation more than $100,000,000 annually.

The methods of sewage treatment developed to prevent water pollution are shown in the film by animated drawings and pictures of the most modern sewage treatment plants in operation. It is pointed out that in 1945 there were 6000 plants in operation, but the Public Health Service estimates that there is a pressing need for more than 10,000 new plants in the country.

Echoes from Bikini

The following, from the *A.A.A.S. Bulletin*, presents some worthwhile thoughts:

> To dwell on the violence of atomic bombs or exploding stars is to miss the real significance of these recent scientific discoveries. Whether or not they will enable human beings to go faster or ascend higher or destroy more of their fellow men matters little in comparison with the assurance that such achievements give human minds that there is a fundamental orderliness in the universe which can be discovered and understood. The awe-inspiring nature of such phenomena as those due to the atomic bomb and storms on the sun or explosions in stars arrests the attention and directs thoughtful minds to deeper questions than the passing problems of the day.
>
> According to messages from Bikini, as reported in the daily press, the atomic bomb was disappointing because it did not make a greater spectacle in the sky, destroy all the ships anchored in the lagoon, and blast away the enclosing atolls. If a demonstration of great forces is what was desired, a telescope and appropriate spectroscopic attachments might have been taken along to make discernible the storms raging on the sun. But the point was not primarily the violence of the atomic bomb and its possible uses in war. It was, rather, the demonstration that, by small-scale experiments on the earth, scientists have confirmed what astronomers had inferred from their observations of storms on the sun and explosions of other stars.

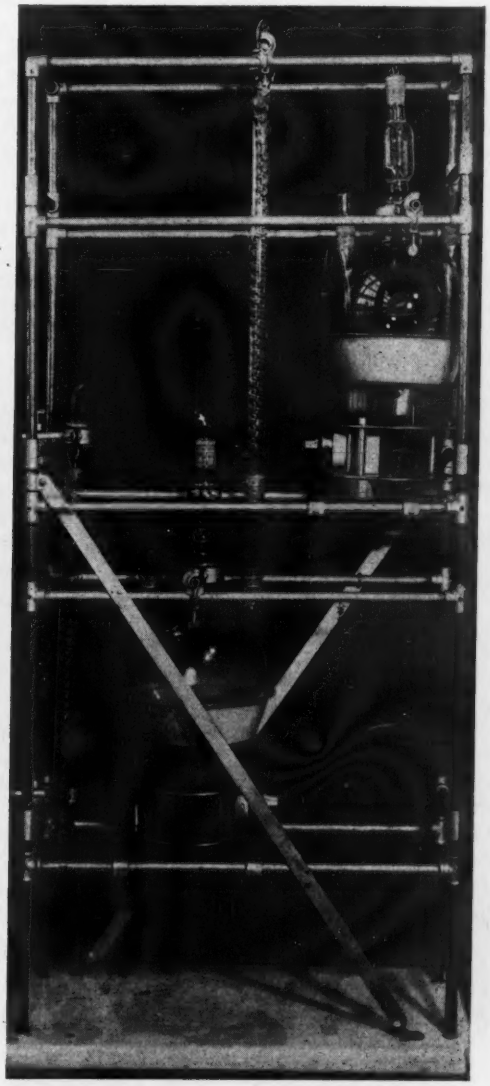
Triple Distilling Apparatus

J. M. Essenberg, of the Chicago Medical School, sends us the accompanying pictures showing some of the details of a rigid steel stand for a triple distilling apparatus. It is 60 × 26 × 10 inches and is constructed of standard $^3/_8$-inch pipe. The horizontal members are threaded into the vertical members and fixed in position with set screws. Some of the details of the clamp construction are shown. The flasks rest in sand-baths on the electric hotplates. The wooden base is mounted on swivel casters for mobility.

Shortage

Demand for trained chemists and chemical engineers is far greater than the supply, William S. Richardson, president of B. F. Goodrich Chemical Company, told the Chemical Institute of Canada in Toronto. "We have need on this continent for a minimum new crop of 10,000 men with degrees in chemistry per year, and it is hoped that those guiding our educational institutions in Canada and in the United States will recognize this need and provide the facilities for such training."

A survey made in 1941 of Canadian chemists and engineers indicates that there were then 3000 persons who could perform any kind of chemical work, and in recent years between 200 and 250 students have graduated each year in chemistry and chemical engineering in 15 Canadian institutions devoted to the study of chemistry, Mr. Richardson said.



In the United States, based on a survey reported April 1, 1944, there were 61,000 chemists, of whom 10,000 had the Ph.D. degree, 13,400 the Masters degree, and 43,500 the B.S. degree in chemistry. In addition there were 20,000 chemical engineers, of whom 750 had the Ph.D. degree, 1900 the Masters degree, and 11,500 the B.S. degree.

"Reports from 376 institutions indicate that there was a total of only 1934 chemists actually in training in the year 1945 to supplement the 80,000 who had in previous years obtained the various degrees, and there were only 462 chemical engineers in training as reported by 86 institutions having an accredited course for that degree in the same year."

Fellowships

The Schenley Research Institute has established at the University of Wisconsin a number of post-doctorate research fellowships for the study of factors affecting the production of antibiotics and their action on human, animal, and plant diseases. They will be applied for the conduct of basic scientific research, the results of which will be published in whatever manner seems, in the judgment of the University, to serve the public interest best.

The field of research for which fellowships have been set up covers the whole cycle of antibiotic production and action—the genetic principles governing the characteristics of producing organisms, the metabolic processes of those organisms, and their manner of action on bacteria, including the development of resistance by bacteria toward antibiotic agents.

In addition to expanding fundamental scientific knowledge in the field, it is also the wish of the sponsors to enable the University to retain the services of first-class research workers for fundamental research against the attractions of industrial employment.

High-Vacuum Leak Testing

A specially designed mass spectrometer that reveals gas leakages so minute that they defied conventional detection methods has been described by engineers of the General Electric Company. The specially developed leak detector can disclose the presence of one part of helium in 200,000 parts of air.

The leak detector is a small portable mass spectrometer, a device which utilizes electric and magnetic fields to sort out ionized gas molecules according to their molecular weight. The instrument continuously draws a sample of gas from the system being leak-tested and indicates the partial pressure of helium in the sample. As portions of the test system are exposed to a helium jet, any helium entering the system through a leak causes an increase in the output current of the amplifier, thus indicating the presence of the leak.

The leak detector may be used to reject defective parts, to locate accurately leaks so that the parts may be repaired, or to aid in selecting production methods and in locating faulty processes. Other applications of the leak detector are methods in which helium may be used as a tracer gas. These include investigation of flow in ventilating systems, velocity and distribution of flow in piping systems, turbulence, and other similar problems.

Crisis in Education

During July, representatives of 40 national associations in higher education, of 75 colleges and universities, of two veterans' organizations, and of governmental organizations engaged in a Conference on Emergency Problems in Higher Education, sponsored by the American Council on Education. Among the 40 or more resolutions adopted by the Conference this may be of particular interest to our readers:

Whereas, the supply of the qualified instructional personnel of universities, colleges, secondary and elementary schools has already fallen far below the current demand and will in all probability create a critically large deficit and a serious impairment of instructional quality by 1947; and

Whereas, this condition threatens failure in the attempt of this nation to provide the promised educational opportunities for veterans, to make up the national deficiency in scientifically trained manpower, and to provide education for world peace for all of our citizens; and

Whereas, this situation has produced an undesirable competition for qualfied instructors between units of the educational system; and

Whereas, necessary instructional replacements of trained persons are being drawn away from education by government and industry, thereby reducing the flow of graduate students into college teaching; and

Whereas, the forces mentioned include such factors as the competition of industry for trained employees, the demands of governmental agencies for staff, the present low faculty salaries, the inadequate housing for school personnel, and the induction of needed educational staff into the military forces:

Therefore, Be It Resolved, 18. That the Commission on Higher Education, appointed by the President, be urged to declare a national educational emergency to exist; to give this matter its immediate consideration; and to recommend solutions.

19. That considering the extraordinary pressure placed upon the colleges and universities by the government's offer of college education for veterans, the American Council on Education be urged to use its full influence to obtain a Selective Service policy of granting occupational deferment for staff members of colleges and universities in fields where critical manpower shortages exist.

20. That the American Council on Education be requested to present data and statistics on critical need of colleges and universities for staff members, calling upon such other agencies as may be helpful in procuring such data.

21. That the American Council on Education be requested to secure continuation of LBM 115 M, providing for consideration for deferment and its extension to fields of teaching and research in which critical shortages exist.

22. That to insure in the long run a fair share of the best talents of the nation be recruited and retained in higher education, every effort of organized education be made, that not only salaries in education be made reasonably competitive with industry and government, but that those inducements offered in the past by academic life, such as freedom of personal action, opportunities for professional service and research, the academic-year appointment, and opportunities to lead advanced students, should be retained or reinstated or *enhanced*.

Quantitative Analysis for Premedical Students

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THERE appears to be a definite need for a separate course in quantitative analysis containing the same general principles of the conventional course but organized in such a manner as to interest the student of medicine. Most colleges offer courses in quantitative analysis to interest the chemist and the chemical engineer without considering the interests of students of other fields. According to a recent article by Van Peursem[1] 30 per cent of the students enrolled in quantitative analysis were premedical students. Twenty-nine per cent were chemists and 30 per cent engineers.

Sarver[2] proposed changes in the customary laboratory experiments by placing emphasis on the analysis of solutions and volumetric techniques which premedical students needed in their medical course.

Special courses are many times criticized as being courses that merely train a student to do a specific laboratory procedure rather than to educate him to apply a principle. This need not be true of the experimental determinations which are chosen to illustrate the basic principles developed. For example, a determination using the iodometric method is considered essential in most courses in quantitative analysis. The chemist may be interested in the analysis of copper ore, while the medical student is probably more interested in the analysis of reducing sugar in urine by the same method. As long as the fundamental principles are the same, a choice of the experiment could be governed by the professional interest of the student.

In view of this interest the author has conducted a survey and tabulated data from 45 of the 67 recognized medical schools in the United States who answered his questionnaire. This questionnaire aimed to determine what medical-school authorities thought was the most valuable content for a laboratory course in quantitative analysis for premedical students. The results showed that authorities unanimously agreed on the desirability of a course in quantitative analysis for premedical students. All but one recommended a course in quantitative analysis for such students, and more than half of them thought that premedical students should not be required to take the same course as those majoring in chemistry. This may be due to the desire of medical faculties to have a course which includes illustrative material of medical interest. But the necessity of a knowledge of the same underlying physical-chemical principles, techniques, and attitudes inherent in an application of the scientific method should be stressed.

The techniques and determinations which the medical schools desire are found in Table 1. They are those encountered in most quantitative analysis courses, and and a few determinations of organic substances.

TABLE 1

DETERMINATIONS AND TECHNIQUES DESIRABLE IN A QUANTITATIVE ANALYSIS COURSE FOR PREMEDICAL STUDENTS

Determinations	*Response*	*Techniques*	*Response*
Sulfate	24	Calibration of pipet	26
Chloride	30	Use of a pipet	31
Acid	36	Calibration of a buret	25
Base	36		
Calcium	25	Use of a standard pH meter	26
Iron	22		
Phosphate	22	Use of a colorimeter	30
Ammonia (Nessler)	25	Use of a saccharimeter	10
Nitrogen (Kjeldahl)	28	Use of a balance	9
Acetone bodies	13	Use of a spectrometer	5
Reducing sugar	17	Use of a refractometer	3
Vitamin C	5	Use of other instruments	9
Other determinations	7		

The apparent current interest among chemistry teachers in the use of a standard pH meter and colorimeter is undoubtedly due to a desire for the students to acquire an additional technique. However, it is obvious that if the student is to make the best use of either instrument, he must know the fundamental principles upon which it is based. With only a few modifications the special course for premedical students may be made to cover the principles found in a conventional course.

In practice, the following experimental determinations have proved to be satisfactory. The sulfate can be determined gravimetrically. Most gravimetric techniques are involved in this determination. The chloride may best be determined volumetrically using one of the adsorption indicators. A solution of almost any weak acid will serve to illustrate the type of acid which a medical student may need to analyze. Experience in further neutralizations may be obtained in an analysis for nitrogen by the Kjeldahl method. Buffer solutions might well be used for pH determinations with indicators or a standard pH meter. Solutions of iron and calcium compounds may be determined by the common method of using either potassium permanganate or ceric sulfate as an oxidizing agent. Reducing sugars may be determined iodometrically by the Shaffer-Hartmann method. The solution of a phosphate is an important determination in which the colorimeter is used.

The principles involved in the determinations are fundamental. The determinations themselves are ones that might interest a medical student.

In conclusion, a special course in quantitative analysis for premedical students seems desirable. Adherence to the fundamental theory and techniques is imperative. The determinations used as illustrative applications may be those which are of interest to the student of medicine. The quantitative analysis course for premedical students taught by the author has been built upon these three generalizations.

[1] VAN PEURSEM, J. CHEM. EDUC., 21, 252 (1944).
[2] SARVER, J. CHEM. EDUC., 7, 365 (1930).

Report of the
NEW ENGLAND ASSOCIATION
of CHEMISTRY TEACHERS

Chemistry and a Life Insurance Company[1]

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THE last decade has seen an enormous change in industrial methods and the introduction into our everyday life of commercial products fabricated with metals, solvents, and plastics of unknown physiological effect on those exposed to their fumes and dusts. This rapid development of industry has made the life insurance companies, who deal in the health and welfare of the population, extremely conscious of a need for better methods of testing the physical status of persons who handle and use these newer materials or who use older materials handled in new ways. Many of the applicants for personal life insurance now come from the so-called "working class," which formerly considered life insurance as beyond its reach. Increased safety measures adopted by industry and the use of modern health programs and life-saving equipment make it unfair to underwrite these applicants by trade alone—yet there must be some choice made between the protected and the unprotected worker. A past industrial exposure that has damaged the applicant is as important in the fixing of a rate of premium scale as the possibility of future hazard, and tests have to be devised so that a choice can be made to exclude those with past damage as well as to detect present danger.

Many of the tests for exposure to industrial hazards can be made by the examining doctor at the time of the physical examination or at a subsequent checkup by special test questions and certain definite clinical signs (wrist drop, blue gum line, chrome sores, perforated septum, etc.). However, a true quantitative test is often required, and this involves laboratory work and chemistry.

Troublesome metals, such as lead, mercury, cadmium, arsenic, chromium, and selenium, have to be particularly noted, and workers with these metals must be given special tests to determine exposure. Such tests for the most part must be rapid, accurate, reproducible, and capable of being performed with the least possible embarrassment to the applicant.

The chemical problems of life insurance chemistry may be classified under two large headings. The first involves the sample—its collection, preservation, and transportation to the laboratory—and the second, the selection and testing of such a sample by a method that is accurate, reproducible, and compatible with the sample. As a life insurance laboratory serves an extremely large territory, samples of urine and blood collected in the field offices must be well enough preserved to hold a glucose solution containing 0.1 gram in 100 cc. of urine from deterioration by mold, bacteria, or yeast for as long as a week in the mails at temperatures as high as 40° C. When this sample is subsequently tested, it must show 0.1 gram in 100 cc.

Samples of blood mailed from as far away as Pearl Harbor and containing 115 mg. of glucose per 100 cc. of whole blood must be received unclotted, unhemolyzed, and show 115 mg. per 100 cc. The request for second samples is time-consuming and often impossible in a competitive business. The use of preservatives or anticoagulants in itself changes the sample by adding new conflicting ions, changing the pH, etc. This makes most of the classical clinical methods found in the literature unusable without adaption and considerable manipulation.

The metals cadmium, mercury, and arsenic, fortunately, are not normal constituents of the urine so that any definite positive tests for these elements is an abnormality and quantitative tests are unnecessary. With lead, however, this is not so; lead is a metal so widely used as solder, paint, spray material, etc., that it is a normal urinary constituent in detectable amounts. Quantitative determinations are necessary in order to see whether the limits of a safety have been reached.

Ingested lead is not so dangerous as lead absorbed through the respiratory tract, so the "dusty" industries are the greatest offenders. Some of the well-known hazardous lead industries are ore handling and crushing, alloy fabrication, lead casting, the pottery trades, glass making, the manufacture of pigments, paint spraying, printing (handling of lead type), gasoline mixing, and farm spraying.

[1] Presented at the Eighth Summer Conference, Middlebury College, Middlebury, Vermont, August 21, 1946.

In the home, lead exposure is usually suspected and discovered only when clinical symptoms develop. Then treatment is started and continued until the patient is more or less symptom-free. The life insurance underwriter wants to know how much lead the applicant is still carrying and how near the danger threshold of clinical poisoning he is. As home exposures are all accidental and unlike the suspected exposures of industries using lead, any control is difficult. Very few people know the type of metal through which their water supply is piped!

The safe limit for concentration of lead dust or fumes in air is "less then 1.5 mg. per 10 cubic meters of air." The extreme dilution of this dust is best visualized by converting the lead to B. B. shot. One B. B. shot weighs about 30 mg. and, if in the form of dust, would be dangerous in a room with a ten-foot ceiling, 35 feet long, and 20 feet wide! The extreme hazard to the workmen occurs in the trades where lead oxide is shoveled in unventilated rooms, where dross is hand skimmed from lead kettles, where lead oxide pigments are dry mixed, and where lead castings are handled in mass production.

As long as this lead is eliminated as rapidly as it is taken into the body, little or no harm is done. Lead elimination seems to cause little kidney damage in subdangerous amounts. As soon as the threshold limit is reached and lead is absorbed faster than it can be eliminated, it is deposited in the tissues, especially in the bones. This threshold limit is usually reached when the lead content of the urine is 0.1 mg. per liter. A urine lead content of 0.2 mg. per liter may or may not cause clinical symptoms but certainly shows a hazardous environment and potential plumbism. Clinical symptoms are usually present when the lead concentration reaches 0.3 mg. per liter.

As urinary lead is lead that has already been circulated in the blood stream and is in the process of elimination, a better picture of the applicant's lead history is obtained from a study of the urine than from that of the blood. In order to combine accuracy and speed of analysis with the use of a small initial sample, a spectograph is used for these analyses. Samples of urine as small as 5 to 10 cc. are used and concentrations of lead in the urine determined as low as 0.08 mg. per liter.

The method consists of the partial removal of organic material by evaporating the sample with redistilled nitric acid. The nitrated residue is taken up in the least amount of water, a measured amount of bismuth salt is added as an "internal indicator," and the sample evaporated in a cup bored in a graphite electrode. This electrode is made the negative pole of a d.-c. arc and the sample activated with 110-volt direct current. The spectrum is registered on a photographic plate.

By the determination of the density of the photograph of the lead line by means of a photoelectric densitometer, the concentration of the lead in the sample may be obtained from a comparison with similar lines made from a sample of known cencentration. The method if properly controlled is good to one part in 10 million.

A routine lead test is performed on urine samples from all applicants for life insurance in the lead-handling industries, and because of this test many persons who work in a potentially hazardous industry are given the benefit of a lower insurance rate than their occupational classification would warrant.

The usual routine of life insurance urine testing as carried out in the life insurance laboratory is a series of quantitative colorimetric tests which have been selected for use because of their accuracy, freedom from complicating reactions with the hundreds of other possible constituents of an unselected specimen, and the ease with which they may be fitted into a routine procedure. Some chemical tests, though reproducible, are inclined to give weighted results and favor either the company's attitude or that of the applicant. False positives and negatives must be suspected and information as to the sensitivity of any test used kept available for underwriting purposes.

The test most used for routine sugar testing is the Benedict picric acid reduction test. In this test a measured amount of urine (of a specific gravity between 1.010 and 1.030) is heated for 10 minutes in boiling water with an alkaline solution of 0.2 per cent picric acid. Glucose reduces the yellow picric acid to the red picramic acid which can be colorimetrically compared to standards. The difference between 100 mg. per liter and 150 mg. per liter can easily be estimated. If there is considerable reduction, the specimen is checked for glucose either by formation of the osazone or by the polariscope.

Actually, for life insurance purposes, any reduction of picric acid is abnormal and so underwritten, but pentosuria and lactosuria are not uncommon. The formation of pentoses (5-carbon sugars) in the metabolism of carbohydrates is interesting as it may be a precursor of diabetes. An applicant whose urine shows an abnormal reduction of picric acid is asked to submit to a sugar tolerance test. This test then determines the insurability of the applicant. Unsuspected diabetes has been found in many cases, and urinary sugars as high as 4000 mg. per 100 cc. and blood sugars as high as 340 mg. per 100 cc. have been detected in people who to their knowledge had never had any trouble.

The chemical testing of the blood of applicants for life insurance has been one of the most important of the laboratory functions. Beside the usual hemoglobin tests for anemia, quantitative determinations of blood for uric acid, nonprotein nitrogen, urea, and blood sugar are routine. Tests are all semimicro in character, as small quantities of blood can most easily be obtained from the average insurance applicant. Either finger prick capillary blood or venous blood is utilized for this purpose.

These blood tests are done only on applicants with history of some impairment, such as gout, renal stones, diabetes, etc., except in cases where the original urine examinations seem to indicate such an impairment.

Statistics based upon data collected over a period of 30 years from thousands of individuals of a mixed age

group seem to show a racial as well as a family tendency toward abnormal sugar metabolism.

As an increased amount of urinary glucose may be caused by any one of several factors (excitement, a specimen taken too near to a carbohydrate meal, so-called "renal glycosuria"—or low carbohydrate threshold), a controlled carbohydrate tolerance test is the only sure method of determining such abnormalities. The procedure is to take a sample of blood from the applicant in the morning before breakfast and then give him a measured amount of dextrose and water. Blood samples are then taken at clocked intervals and the time-concentration curve of their sugar content plotted. A normal curve is one that starts at about 100 mg. per 100 cc. and though it may have a high initial peak of 185 mg. per 100 cc., it drops down to below 160 mg. per 100 cc. in about an hour and a half. If the time intervals are accurately taken, two samples are enough for life insurance purposes—a fasting specimen and one at an hour and a half. By the Folin method the test is performed with 0.1 cc. of blood and with reproducible accuracy—at least with an accuracy good enough so that the company has over 50 million dollars worth of business based on this test alone, and the experience with this business over the past 18 years has been better than that of standard business. The test is colorimetric and involves the formation of ferro ferricyanide by the reduction of ferricyanide by the glucose in the blood. Blood samples for such tests are sent into the laboratory from all over the country with the blood preserved against clotting and decomposition by means of a mixture of thymol and sodium fluoride. This preservative works well but constantly interferes with the chemistry of the ordinary clinical tests listed in the literature, which were designed for fresh citrated or oxalated blood. By revising the test through the use of a suitable control of the acidity, a method has been adapted which works on blood that is often a week old and has been submitted to all the vagaries of temperature possible in a mail pouch.

In addition to the routine urine and blood chemistry on specimens submitted by applicants for the various types of life insurance, the laboratory of the medical department is utilized by the other departments and companies in the affiliated group as a source of information. Questions concerning water analyses, ink spot removal, and all the other thousands of kinds of pseudo-scientific umbrella mending that are found to be the heritage of any chemist are, of course, brought to the laboratory of a life insurance company. But fortunately, added to these uninteresting chores, are a great group of interesting problems, more or less chemical in nature, that originate with the other lines of insurance written by the parent company. These problems are so foreign to the unsolved mysteries of preservatives and pH that they are welcomed with open arms.

One problem received before the war involved the shipment of lard to England. Upon arrival at its destination it was found to be packed in mildewed containers, and the shipment was refused. A sample of the container was brought to the medical laboratory for investigation. We were able to grow and identify the mold that was causing the mildew and, by the cooperation of the box manufacturer, to show that the spores for this mold were present and viable in the glue with which the box was fabricated. The claim was subrogated and the insurance company that insured the glue company paid for the repacking of the lard.

Another problem concerned a cafeteria. One of the bakers discovered a handful of broken glass in the bottom of the mixing bowl just after filling 23 pies with pumpkin filling. As a safety measure all the pies were destroyed. Fortunately the glass was saved, as the next day glass chips were found in a casserole of cod fish combination. This aroused the suspicion of sabotage, as the bakers of the pies and the cooks of the fish had no utensils in common nor did the personnel overlap. The first thought was glass in the milk, for milk was the common ingredient, although none of the glass had the curvature of a milk bottle. A third piece of glass then was discovered in a serving of chicken and noodles. There was no milk used in this preparation. Samples of the glass found were sent to the laboratory, and a spectrographic comparison was made; there were three types of glass evident from this analysis. A relative refractive index was determined by powdering the glass and suspending it in a mixed oil. By looking at the specimen in the oil under the microscope and thinning the oil with a suitable solvent until the visible edge of the particle disappeared, a difference in refractive index was apparent. There were three different pieces of glass. This led to the one solution possible to the laboratory: that there were three accidents, if they were accidents, and that an investigation was advisable. A study of the cafeteria was made by a trained inspector, and it was evident that at least three things were at fault—none of them sabotage and each easily corrected: a general housecleaning and removal of old mayonnaise jars from precarious positions around the kitchen; the use of paper drinking cups at a special drinking place; the delegation of "clean-up" authority to some one competent member of the staff. As far as is known no further trouble occurred.

An oatmeal breakfast cereal was insured for products' liability. After several claim-free years there was suddenly a whole series of complaints—grocers were getting the cereal returned because of a peculiar odor noticed during the preparation of the breakfast food by the housewife. A sample was sent to the Home Office for investigation, and in due course the medical laboratory was consulted. The odor had been identified as furfurol, and it was believed that a mold was a contaminant.

Examinations of the cereal under the microscope showed abundant hyphae, and upon moistening and incubating a portion, various molds grew abundantly. *Mucors, aspergilla,* and *penicillum* were identified. A box of similar cereal was purchased in the local grocery store, since mold contamination in the opened box enroute to the laboratory was quite possible, and a sealed

box if found contaminated would rule this possibility out.

This cereal also grew mold spontaneously when moistened in the laboratory. There had been no reports of spoilage from the local district, so it was fairly well established that either moisture and heat were necessary to incubate the mold or a time lapse was required between factory packaging and the time the customer used it. The cereal company checked the sales calendar of the grocery firms through which the complaints had come. It was found that in all cases the cereal stock had spent a matter of six or seven months in storage before sale. By treating the product as a perishable food—which it certainly was, as it had been partially cooked in the preparation process—the furfurol odor and mold contamination were removed and as far as is known there has been no more trouble.

A factory making small electrical coils for the electrical mechanism that activates the machine guns in the wing tips of a fighter plane suddenly noticed a prevalence of authenticated illnesses among the girls who sprayed the small coils of wire with lacquer. Physical examinations with blood tests were ordered on the members of the department and a complete study was made. Of the 14 girls involved only one had a normal hemoglobin. This seemed to indicate a hazard of some duration. It was found by the inspection engineers that the room in which the coil spraying was done was suitably exhausted and the spraying was all done in forced-draft hoods. However, due to war shortages the polymerizing finish formerly used had been changed to a cellulose acetate type which hardened not by polymerizing but by evaporation of a solvent. The coils were hung on a "temporary" clothes-line type dryer, and the 30 or more gallons of solvent used each day allowed to evaporate spontaneously into the room. The exhaust fans could not clear the room fast enough. The plant management ordered an immediate change in the process. The girls were followed by tests for three months and all quickly returned to normal.

Since several claim problems had involved molds, the insurance adjustors began to think that *all* claim problems could be solved through the growth of a few dishes of fungus. A cargo of canned fruit and vegetables in a refrigerator boat, after being unloaded on the dock in the hot sun, were stored in the warehouse where in time the labels developed dark stains. The claim adjustor sent in several samples with the suggestion that the label glue be tested for molds. The stains were easily proved to be iron rust from the can. It was believed that the tinning must be at fault, as each stain on the paper label occurred over a marked striation in the protective tin coating of the can. These striations were all longitudinal, suggesting defects in the tin sheet or the fabrication. It was then found that the tin sheet was insured from Wales to the consumer under six different ownerships, and at least eight different insurance policies—each with our company! As any subrogation of the original claim would be merely bookkeeping, the original claim was paid.

From those few examples it can be seen that although much of the chemistry in a life insurance company is routine, the work is diversified. No two days are alike, and no two mails bring in the same problems. Newer methods must be constantly tried and new tests adapted to insurance work.

SCHEDULE OF MEETINGS

237th meeting, October 19, 1946, Colby Junior College, New London, New Hampshire.

238th meeting, December 7, 1946, Boston College, Boston, Massachusetts.

239th meeting, February 15, 1947, Rumford Chemical Works, Rumford, Rhode Island.

240th meeting, March 22, 1947, Trinity College, Hartford, Connecticut.

241st meeting, May 10, 1947, College of the Holy Cross, Worcester, Massachusetts.

Air can be dried or moistened in exactly the same way—by blowing it through water sprays. The big difference is in the temperature of the water, the chilled variety serving to dry it, while warm-water sprays raise the humidity to a comfortable level.—Westinghouse Newsfront (July-August, 1946).

RECENT BOOKS

ADVANCES IN COLLOID SCIENCE. Vol. II: Scientific Progress in the Field of Rubber and Synthetic Elastomers. Edited by *H. Mark* and *G. S. Whitby*. Interscience Publishers, Inc., New York, 1946. xi + 453 pp. Illustrated. 15 × 23.5 cm. $7.00.

This is the second volume of a series which was inaugurated in the United States by the late Elmer O. Kramer, one of the pioneers of colloid chemistry. It will always be a fitting memorial to him.

This volume contains the following contributions: "Second-Order Transition Effects in Rubber and Other High Polymers," by R. F. Boyer and R. S. Spencer; "Crystallization Phenomena in Natural and Synthetic Rubbers," by L. A. Wood; "The Study of Rubber-like Substances by X-ray Diffraction Methods," by C. W. Bunn; "The Thermodynamic Study of Rubber Solutions and Gels," by G. Gee; "Significance of Viscosity Measurements on Dilute Solutions of High Polymers," R. H. Ewart; "The Kinetic Theory of Rubber Elasticity," by E. Guth, H. M. James, and H. Mark; "Vulcanization," by E. H. Farmer; "Rubber Photogels and Photovulcanizates," by H. P. Stevens; and "Reinforcing and Other Properties of Compounding Ingredients," by D. Parkinson.

There is a great amount of very valuable information contained in this volume written by men whose names are well-known in the fields of their contributions. However, the reviewer feels that either the book should not have been made part of the series "Advances in Colloid Science," or topics of more general interest to the colloid chemist should have been included.

The rubber chemist will definitely profit by studying this book; the chemist interested in synthetic resins might find some valuable information, but the less specialized colloid chemist will be disappointed.

It is interesting to note that out of the total of nine papers assembled in this volume, five have been contributed by British scientists.

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POISONS. *Vincent J. Brookes*, Sergeant, New Jersey State Police, and *Hubert N. Alyea*, Associate Professor of Chemistry, Princeton University. D. Van Nostrand Company, Inc., New York, 1946. xv + 209 pp. 14 × 22 cm. $3.00.

A large share of the book is devoted to alphabetically arranged descriptions of poisons that are common in the home, in industry, and in therapy, together with symptoms and treatment. This might possibly be of aid to police officers, chemists, and other laymen, providing they had studied it thoroughly previous to an emergency. The descriptions are, however, cluttered up with unused synonyms, sketchy methods of manufacture, incomplete dosage forms, and chemical identifications that are either unusable by laymen or useless in emergencies. The descriptive lists, together with tabular summaries, a chapter on poisoning from foods, plants, snakes, and spiders, and one on special techniques in treatment, comprise five of the seven chapters, about 70 per cent of the book.

The balance contains usual pertinent information and much that is superfluous. The two introductory chapters give definitions, general symptoms and treatment, and first aid. They also attempt to induct the layman into the mysteries of chemistry in three pages, including symbols, formulas, and equations in words, and to prepare him for chemical identifications by simple tests. In the appendix is a weird glossary of words, a large share of which are familiar to all school children; a few examples are metallic, variable, opaque, retard, substance, solid, intense, edible, dilate, and fabric. The rest of the appendix gives a list of reagents and apparatus and an extensive table of weights and measures.

The preface states that this was "originally written for police, investigators, and peace officers," but the material, "we believe, will be of value to physicians, nurses, chemists, and pharmacists. It would even be valuable in the home." Undoubtedly a police officer, who is often first at the scene of a poisoning, needs all of the help that he can get, and perhaps this volume could give him some aid. However, to think that any of the material could be of any value to pharmacists, nurses, or physicians is almost absurd; expecting lay authors to instruct professionals in their own fields is certainly naive.

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TECHNIQUES OF GLASS MANIPULATION IN SCIENTIFIC RESEARCH. *Julius D. Heldman*, Chemistry Department and the Radiation Laboratory, University of California. Prentice-Hall, Inc., New York, 1946. xii + 132 pp. 56 figs. 15 × 23 cm. $3.60.

In any craft there are apt to be several ways to attain a given result. The dispassionate observer viewing the completed works may suspect that these methods are of nearly equal worth or, at any rate, that they can all be made to work. Not so the craftsman. Usually he will contend vigorously that only one of these methods could be used by any man of honor and rectitude. This is as true of glass-blowing as of sculpture.

Dr. Heldman's book is not a compendium for the professional, but a small volume for the amateur. Since, of necessity, he can give but one or a few of the possible procedures, the experienced glass blower may look in vain for his pet method. But the methods given are reasonable and practical ones and should give the beginner as good results as any others. Procedures lean to the use of cross-fires instead of cannon-fires. The new silent burner is not used.

Commencing with equipment and the properties of glass, the text proceeds through basic operations to simple seals and finally to finished equipment exercises. Treatment is determined by current laboratory requirements and is thoroughly modern. A chapter on the use of the hand torch on mounted apparatus is included. Save for a short section on fused silica, glasses other than borosilicate (Pyrex) are treated only in connection with glass-to-metal seals. The section on such seals is particularly good.

After the years of wartime restrictions on printing, it is a pleasure to see a book so handsomely turned out. The attractiveness of the page is increased by large margins and twelve point type. A year ago this book would have been printed on hardly half so many pages. Yet it must be acknowledged that this must contribute to what seems a rather steep price, even today, for a volume of comparatively few words. The line drawings and photographs are excellent. A glossary of glass-blowing terms and an index are provided.

"Glass Manipulation" and a little assistance from a glass blower should enable the novice to develop reasonable facility in the art. The advanced amateur and even the professional will pick up suggestions of value. But any good book on glass blowing inevitably presents the danger of encouraging one to make apparatus better left to the laboratory glass blower on considerations of efficient utilization of research time.

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